Pediatrics

OFFICIAL PUBLICATION OF THE AMERICAN ACADEMY OF PEDIATRICS, INC.

VOL. 9 FEBRUARY 1952 NO. 2

Editorial Board

ALLAN M. BUTLER, Boston
HAROLD K. FABER, San Francisco
ALTON GOLDBLOOM, Montreal
PAUL A. HARPER, Baltimore
L. EMMETT HOLT, JR., New York
RUSTIN MCINTOSH, New York
HERBERT C. MILLER, Kansas City, Kan.
RALPH V. PLATOU, New Orleans
MITCHELL I. RUBIN, Buffalo
FRANCIS F. SCHWENTKER, Baltimore
MILTON J. E. SENN, New Haven
JOSEPH STOKES, JR., Philadelphia

Contributing Editors

JOHN P. HUBBARD, Philadelphia
MYRON E. WEGMAN, New Orleans
FEDERICO GÓMEZ, Mexico, D. F.

HUGH MCCULLOCH, *Editor*
La Rabida Jackson Park Sanitarium, Chicago 49

Ex Officio

WARREN W. QUILLIAN, *President*, Coral Gables, Miami, Fla.
EINOR H. CHRISTOPHERSON, *Executive Secretary*, Chicago

CONTENTS

ORIGINAL ARTICLES:

Some Aspects of the Chemical Composition, Physiology and Pathology of Intracellular Fluid—*William M. Wallace, M.D.* 141

Anomalies of the Pulmonary Veins and Their Surgical Significance; Report of Three Cases of Total Anomalous Pulmonary Venous Return—*Harry G. Parsons, M.D., Ann Purdy, M.D., and Bruce Jessup, M.D.* 152

Paroxysmal Tachycardia in Infants and Children; Study of 41 Cases—*Alexander S. Nadas, M.D., C. William Daeschner, M.D., Arthur Roth, M.D., and Stanley L. Blumenthal, M.D.* 167

Coagulation Studies in the Newborn Infant. I. Normal Infants—*Burton J. Grossman, M.D., Ruth M. Heyn, M.D., and Irving H. Rozenfeld, M.D.* 182

Brain Abscess Associated with Congenital Heart Disease—*Regina Gluck, M.D., John W. Hall, M.D., and Louis D. Stevenson, M.D.* 192

Hypotonic Cerebral Palsy in Mental Defectives—*Herman Yannet, M.D., and Frank Horton, M.D.* 204

(Contents continued on page iv)

CONTENTS

(Contents continued from page iii)

Further Studies on the Influence of Histamine on Platelet Activity, with Especial Reference to Its Action on the Blood of the Hemophiliac Patient—*Heyworth N. Sanford, M.D., F. Richard Hall, M.D., and Stuyvesant Butler, M.D.* 212
Localized Hypertrophic Emphysema—*Robert R. Shaw, M.D.* 220

AMERICAN ACADEMY OF PEDIATRICS:

The President's Page—*Warren W. Quillian, M.D., President* 228
Summary Report: Regional Pediatric Conferences, 1950-51 230
Symposium on Physiological Consideration of Respiratory Disease—*Julius H. Comroe, M.D., Chairman* 233
Round Table Discussion: Prevention of Accidents in Childhood—*George M. Wheatley, M.D., Chairman* 237

SPECIAL SECTIONS:

The Pediatrician and the Public—*Paul A. Harper, M.D., Editor. Communication from Phillip E. Rothman, M.D.* 243
TRENDS—*John P. Hubbard, M.D., Contributing Editor* 249
Public Health, Nursing and Medical Social Work—*Myron E. Wegman, M.D., Contributing Editor.* Health Services for School Children—Priorities and Program 252
News and Announcements 259
Book Reviews 261

PEDIATRICS is owned and controlled by the American Academy of Pediatrics, Inc. Entered as second-class matter March 13, 1948, at the postoffice at Springfield, Illinois, and Menasha, Wisconsin, under the Act of March 3, 1879.

Copyright 1952, by the American Academy of Pediatrics, Inc. Printed in U.S.A.
Copyrighted in the British Commonwealth by Blackwell Scientific Publications, Oxford. No part may be duplicated or reproduced without permission of publishers.

TWENTIETH ANNUAL MEETING
The American Academy of Pediatrics
October 18 to 23, 1952
Palmer House
Chicago

AREAL MEETING
May 22 to 24, 1952
Statler Hotel
Washington, D.C.

Pediatrics

VOLUME 9 FEBRUARY 1952 NUMBER 2

ORIGINAL ARTICLES

SOME ASPECTS OF THE CHEMICAL COMPOSITION, PHYSIOLOGY AND PATHOLOGY OF INTRACELLULAR FLUID

By WILLIAM M. WALLACE, M.D.
Boston

I ACCEPT the Mead Johnson Award for 1951 with gratitude tempered with the sense of the future obligation that your choice imposes. The preparation of a presentation such as this accentuates the realization of how many of one's own thoughts are but those of others phrased in the terms of individual experience. The present award must be considered as given to many. Dr. James L. Gamble has pointed to the problems and, by his presence and work in the laboratory, provided the stimulus and guidance for pursuing the work to be discussed. Dr. Charles A. Janeway has carried the difficult and unseen and, so often, unthanked burden of seeking and providing the means for carrying on the work and, by his wide field of interest and knowledge, suggested many of the ideas pursued. To my contemporaries in the laboratory, Dr. Jack Metcoff, Dr. Leonard Eliel, Dr. Malcolm Holliday, Dr. Robert Schwartz, Dr. Ernest Cotlove, Dr. William Schwartz, Drs. George and Nancy Nichols and Dr. William Bergstrom must go the credit for the great bulk of the work done. Any credit that may accrue must also be shared with those who did so much of the analytic and secretarial work and provided the nursing care in the clinical studies. Work of the type to be discussed requires substantial financial support and appreciation must be expressed to the Mead Johnson Company, the United States Public Health Service and the Grant Foundation for supplementing the liberal opportunities for research at the Children's Medical Center.

E. Mead Johnson Award Address, read at the Annual Meeting, American Academy of Pediatrics, Toronto, Oct. 24, 1951.

From the Department of Pediatrics, Harvard Medical School, and the Children's Medical Center, Boston.

Aided by grants from the Mead Johnson Company, the National Heart Institute, of the National Institutes of Health, Public Health Service and the Grant Foundation.

(Received for publication Nov. 19, 1951.)

It is the purpose of this paper to consider some concepts of the electrolyte composition, physiology and pathology of the intracellular fluid and to inquire into their application to clinical problems. While therapeutic procedures specifically directed toward the intracellular fluid will never have the dramatic effectiveness that results from the administration of water, salt and blood, they are assuming increasing clinical importance as progress in the use of chemotherapeutic agents, surgery and endocrine therapy widens and, at the same time, multiplies the complexity of therapeutic possibilities.

Chart 1 is shown to indicate the water, solid and electrolyte composition of interstitial fluid, connective tissue and intracellular fluid, the latter as exemplified by muscle cells. Each block represents a kilogram of the phase. Along the abscissa the clear area

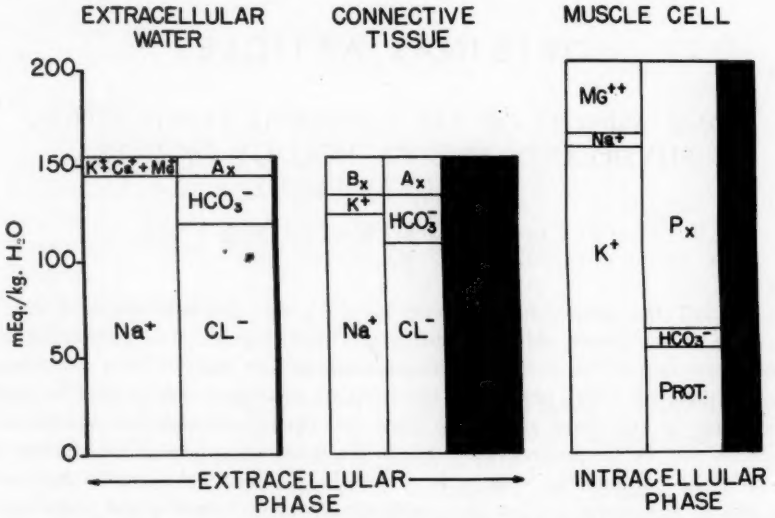


CHART 1. Electrolyte, water and solid content of kg. of extracellular fluid, connective tissue and muscle cells. Black areas indicate solids of 1 kg. and clear area water of tissues. Extracellular fluid concentrations were calculated from standard serum values, connective tissue diagram taken from Manery, Danielson and Hastings,[2] muscle cations from Cotlove and associates,[10] muscle anions calculated from literature.

represents the water and the black area the solids of the phase. The height of the block indicates the concentration of various electrolytes in the water phase. On the left is shown the well known composition of interstitial fluid, a plasma ultrafiltrate. The center block depicts the composition of the connective tissues of the body as found in tendon and fascia. The similarity, except for its solid content, to extracellular water is evident. Chemical investigation of these supporting tissues indicate that the Na, Cl and HCO_3' ions contained in their water are in ionic equilibrium with blood plasma. Their concentrations vary passively and directly with changes in plasma concentration of these ions. For example, in adrenal insufficiency, when the Na and Cl of the plasma are lowered, the concentration of these ions in connective tissue will be lowered in a parallel fashion.[1] As Manery, Danielson and Hastings[2] have pointed out, the extracellular phase of tissues must be considered to be an ultrafiltrate of plasma diluted with connective tissue.

TABLE 1

WATER AND ELECTROLYTE AND SOLID COMPOSITION OF MAN
(Dilution Technics)

	Mean	Range	Method	Source
H_2O	61.8% wt.	55.9–70.2	D_2O Dilution	Schloerb et al., J. Clin. Investigation **29**: 1296, 1950
Fat	15.6% wt.	23.6– 3.8	$100 - \frac{\%\,H_2O}{.732}$	Pace and Rathburn, J. Biol. Chem. **158**: 685, 1945
Na	40.7 mEq./kg.	32.0–54.0	Na^{24} Dilution	Forbes et al., J. Clin. Investigation **30**: 558, 1951
Cl	30.0 mEq./kg.	25.8–35.2	Br Dilution	Dunning et al., Proc. Soc. Exper. Biol. & Med. **77**: 854, 1951
K	46.3 mEq./kg.	37.0–57.0	K^{42} Dilution	Corsa et al., J. Clin. Investigation **29**: 1280, 1950
Inulin Space	16.0% wt.	—	Inulin Dilution	Levitt et al., Am. J. Med. **9**: 208, 1950
			(Direct Analysis)	
H_2O	59.0% wt.	—	Desiccation	Taken from Shohl, A. T., Mineral Metabolism, American Chemical Society, Series 82, New York City, Reinhold Publishing Corporation, 1939.
Fat	18.0% wt.	—	Analysis	
Fat-Free Dry Wt.	23.5% wt.	—	Desiccation	
Bone Solids	10.0% wt.	—	Analysis	
Na	34.5 mEq./kg.	—	Analysis	
Cl	30.0 mEq./kg.	—	Analysis	
K	49.0 mEq./kg.	—	Analysis	

The electrolyte pattern of muscle, free of extracellular phase, is seen to be altogether different from that of the extracellular phase structures. Potassium makes up the bulk of the cation and phosphate and protein the bulk of the anion. Unlike the extracellular phase, the concentration and pattern of the intracellular electrolyte are dependent upon metabolic activity of the cell and are only indirectly linked to those of the extracellular phase. This conception of intracellular composition of muscle has been derived using the assumption that the chloride in this tissue is entirely extracellular. The evidence for the essential correctness of this assumption for muscle has been summarized by Hastings.[3] Certain cellular tissues, notably the erythrocytes, contain chloride that is morphologically intracellular yet is functionally a part of the extracellular electrolyte in that it is in ionic equilibrium with blood plasma. Since muscle water makes up the great

bulk of the actively metabolizing tissue of the body, it will be the greatest determinant of intracellular fluid in terms of total body composition.

Since the tissues are relatively inaccessible to the clinical investigator, information concerning the composition of the intracellular phase in the living subject must be obtained by indirect means such as balance determinations of water and electrolytes or by determining the volume distribution of injected substances. Table 1 contains a representative collection of data from the recent literature giving mean values obtained by dilution technics in man for water, fat, Na, K, Cl and extracellular space as measured by the volume distribution of inulin. For contrast, the collected values given by Shohl[4] as obtained by total body analysis are also shown. The agreement is generally good, considering the small number of analyses available for the directly determined values. The directly determined value for Na is probably most suspect because of the analytic methods employed.

The dilution data given in table 1 may be used to calculate the volume and electrolyte composition of the intracellular fluid of the whole body in two ways. If the sum of inulin space, water-displacing fat and bone solids is subtracted from the whole, the intracellular phase of the body represents 59%, and contains 45.8% of the body water. Assignment of the nonfat and nonbone solids to the intracellular phase gives a phase containing 78% water, about that found in muscle by direct analysis. Assignment of the noninulin space Na, Cl and K to the intracellular water, however, gives a Cl concentration of 26 mEq./l., a Na concentration of 38 mEq./l., and a K concentration of 100 mEq./l., a composition very different from that shown for muscle in chart 1. A second method of calculation of intracellular fluid volume and electrolyte concentration is to use the assumption, valid for muscle, that chloride is an extracellular electrolyte and is in Donnan equilibrium with plasma water. Chloride then defines the interstitial water plus the total body connective tissue, a tissue in which the bulk of the electrolyte appears to function physiologically as though it were a part of the extracellular fluid. The possibility that this second method of interpretation is a valid one is supported by tentative data of Kruhöffer[5] indicating that inulin only partially penetrates the water of dense connective tissue-like tendon. Preliminary data of our own also indicate that the chloride space of connective tissue is considerably greater than the inulin space.[6]

Chart 2 has been constructed in this way using the data of table 1 and the assumptions that inulin penetrates 15% of connective tissue and that chloride measures the interstitial water plus connective tissue. In this conception of the distribution of total body electrolyte between extra- and intracellular fluid the ionic concentrations are similar to that shown for muscle in chart 1. The extracellular phase in such a conception is no longer than that of a purely water phase but one with a definite structural organization. It should be borne in mind that such formulations of total body composition are highly theoretic and statistical. In addition, they are essentially static ones, they do not take into account the varying rate of distribution of injected substances with physiologic state, the varying rates of penetration of labelled molecules into phases of the body such as bone, the exchanges with the intestinal tract and the glandular lumina nor the passive exchanges of chloride between serum and erythrocytes. The primary purpose of presenting this concept is to indicate the need for distinguishing intra- and extracellular electrolyte on the basis of physiologic behavior rather than morphologic distribution.

Chart 2 indicates the need for considering body build in assessing situations involving losses of water and electrolyte from the body. Body fat represents a water-free phase and

may vary between a few per cent to 35% or more of the body weight with inverse variation of water and electrolyte content. The acute loss of 10% of body weight in a child with a 5% fat content would represent a 14% loss of body water, while the loss of 10% of body weight from a child with a 35% fat content would represent a 20% loss. The clinical observation that obese infants stand dehydration less well than lean ones find its basis in these considerations.

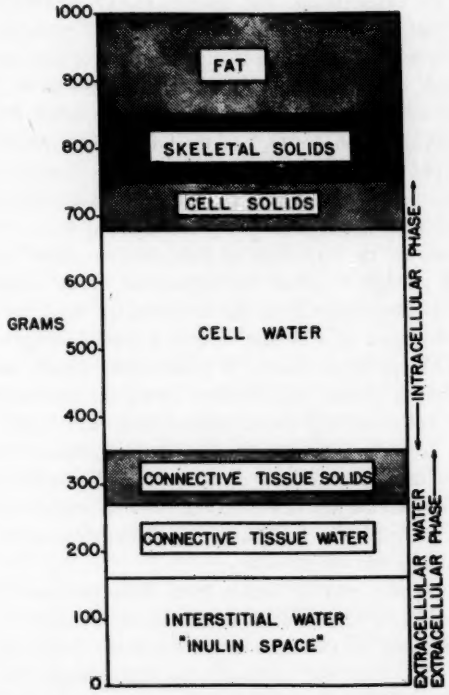


CHART 2. Schematic diagram to indicate water and solid distribution in hypothetic kg. of man. Data are derived, as indicated in text, from that in chart 1 and table 1. Volume occupied by plasma is included in "inulin space."

These possibilities for the interpretation of balance and dilution data indicate some of the difficulties that face the clinical investigator in the attempt to define the variations that occur in the volume and composition of extra- and intracellular fluid during the changes that take place in disease. Setting aside these difficulties, we should like to review briefly certain of the interrelationships between the individual extra- and intracellular electrolytes in which our laboratory group has been interested.

Inorganic and organic phosphate and protein constitute the bulk of the anions of intracellular fluid where they form the basis for the metabolic activities of the cell. In the last analysis the distribution of water and electrolytes depends upon their variation with metabolic activity. Despite this, little is known concerning this relationship, although they have been studied intensively from other points of view. A beginning in this direction has been made by Guest and Rapoport.[7] The greater height of the total base con-

centration in intracellular fluid over extracellular fluid shown in chart 1 suggests inequality of total ionic concentration in the two phases. The multivalency of these anions explains the discrepancy without the need for invoking osmotic inequality.[8, 9] Extra- and intercellular total base concentration may vary quite independently by virtue of changes in the state of activity of the anion.[10]

Reference to chart 1 shows that the bicarbonate content of intracellular fluid is approximately half that of the extracellular. The ratio of H_2CO_3 to HCO_3' in cellular water is approximately half that of the extracellular, indicating a probable intracellular pH of about 6.8 in muscle water. During acute changes in the acid base balance of extracellular fluid the concentration of intracellular HCO_3' is independent of changes in the extracellular concentration of this ion. Rapid elevation of the serum HCO_3', if accompanied by elevation of the CO_2 tension (pCO_2) of the body fluids, results in a decrease in calculated intracellular pH while changes in bicarbonate ion unaccompanied by changes in pCO_2 result in little change in intracellular pH.[11] Intravenously administered HCO_3' appears to be limited in its distribution to the extracellular fluid.[12] One interpretation of these observations may be that transfers of base between intra- and extracellular fluid cannot occur rapidly enough to allow for adjustment of the intracellular buffer equilibrium when the acid-base balance of the extracellular fluid is rapidly shifted. Even during prolonged disturbance in acid-base balance a similar independence between intra- and extracellular HCO_3' probably occurs. In K-deficient animals, when the extracellular fluid base concentration is normal and alkalosis exists, the concentration of intracellular base and HCO_3' are both low and the calculated intracellular pH is below the normal range.[13] Until more is known concerning how the intracellular buffer anion changes with pH, a definitive description of the acid-base equilibrium within intracellular fluid is impossible. The observations just described do, however, indicate that the determinants of the acid-base system in the two fluids achieve considerable independence by virtue of their different distributions and diffusibilities.

Certain guiding principles may be drawn from these considerations. If attempts are made to administer alkali rapidly in amounts calculated to restore the serum HCO_3' the calculation should be based on extracellular fluid volume rather than total body water. Furthermore, since pCO_2 does not necessarily parallel changes in HCO_3', serum pH, representing the ratio of HCO_3' to pCO_2, will be a clearer guide to therapy than will serum CO_2 content (or combining power). This measurement will be the most sensitive indicator of over-treatment and will provide the best measure of the quickly adjustable component of intracellular acid-base balance. During rapid alkali therapy respiratory adjustment lags behind the rate of base administration. In diabetic acidosis the hyperpnea generally persists despite the administration of alkali and serum pH is disproportionately elevated in comparison with HCO_3' concentration.[14] In this instance pCO_2 will remain the same or even be lowered and the effect on intracellular pH will be minimal. On the other hand, as so often occurs in severely sick infants, the respiratory response to acidosis is minimal. Little or no rise in serum pH will occur, indicating that, while HCO_3' concentration is increasing, pCO_2 is rising disproportionately and intracellular pH can be expected to decrease. These mechanisms may explain the variable clinical response seen following alkali therapy. Ultimately correction of acidosis cannot be complete until respiratory adjustment is normal and the intracellular fluid obtains its necessary complement of base (K) and anion.

Magnesium occurs in relatively high concentration in intracellular fluid where its presence is essential to the phosphorolation reactions of carbohydrate. In a study recently carried out in our laboratory upon the effect of changes in acid base balance, potassium deficit and magnesium deficit, upon the amount of this ion in muscle little change of this component of intracellular fluid was found.[10] Even prolonged dietary deficiency of Mg failed to produce significant changes. A suggestive finding in these experiments was a large reduction in intracellular K concentration associated with dietary Mg deficit in animals supplied with an abundant K intake. Losses and gains of Mg in excess of that to be expected from the loss or gain of protoplasm have been shown to occur during the development of diabetic acidosis and during recovery.[15,16] In view of the relatively stable state of Mg in muscle during periods when transfers of electrolyte are occurring between body compartments, we are inclined to the view that the gains and losses of this ion demonstrated by balance methods are probably referable to gain and loss from bone matrix, the largest site of body Mg.

The mechanism by which the concentration of K in intracellular fluid is maintained and Na relatively excluded, despite large concentration gradients, has been a subject of intensive investigation for years. A unified concept, acceptable to all, to explain the separation has not been forthcoming. Extensive reviews of this subject, primarily from the point of view of the cell physiologist, are available.[17-19] One point of view is that the relationship may be adequately explained on the basis of known principles describing the distribution of ions across semipermeable membranes. A second point of view, one that seems to fit best the complex behavior of Na and K in the living intact subject, is that the separation is accomplished by the metabolic work of the cells themselves. Other than their purely physiologic interest, such exchanges are of clinical importance in that they produce symptoms, chiefly with regard to disturbances in acid base balance and in the function of cardiac muscle. The work of Buchanan and Hastings[20] indicates that cellular enzymatic processes cannot be fully efficient unless proper concentrations of K are maintained in intracellular fluid. The essential features of such an exchange, viewed with regard to the economy of the whole body, rather than the isolated cell, have been summarized by Darrow[21] as follows: ". . . . it seems rather clear that there is a biological equilibrium or biological steady state in which three variables (intracellular Na and K and serum HCO_3') bear predictable relationships to each other, when renal function is carried out in the presence of deficit of one of the ions—Na, Cl or K. The biological equilibrium may be initiated either by primary change in serum HCO_3' or muscle K and is the same in normal and adrenalectomized rats." Thus when alkalosis (relative deficit of Cl) exists intracellular K concentration will be low and Na high. In acidosis the reverse will hold true. Adjustment of the equilibrium is essentially dependent upon adequate renal function.[22] It should be emphasized that the relations just described are those seen in experimental animals with normal renal function and primarily single deficits of one of the ions concerned. In most clinical conditions ion deficits are multiple and complicated by changes in renal function, by dehydration and by abnormal metabolic activity. Here the equilibrium is not maintained and they should be considered, as Darrow has pointed out, unstable states.[21] It is only when repair of the unstable state is attempted that the equilibrium may become evident and then only if repair has not replaced the multiple deficits. This is seen particularly well in diabetic acidosis. Such patients have, when first seen, loss of body K, acidosis and often an elevation of serum K con-

centration—the equilibrium is not maintained. Treatment of the metabolic abnormality by repair of dehydration and the use of insulin reverses the unstable state and, unless repair is complete, alkalosis and a low serum K concentration will appear. Administration of K to the patient in diabetic acidosis without the administration of insulin will only accentuate the conditions.

Chart 3 presents an illustration of how changes in acid-base equilibrium may effect the distribution of body potassium. The data were obtained by Dr. William B. Schwartz during a study of the action of mercurial diuretics.[23] The observations are of interest for

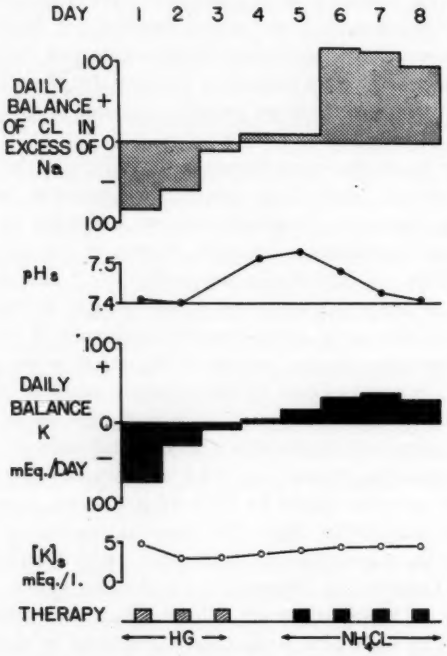


CHART 3. Relation of Cl and K balance to acid-base equilibrium during mercurial diuresis.

the present discussion in that they provide an illustration of the effect of such changes in both directions in the same subject; one is not left, as is so often necessary in clinical investigation, with only the surmise that recovery mirrors the development of the condition. A frequent accompaniment of mercurial diuresis is the renal excretion of Cl in excess of Na with consequent production of hypochloremic alkalosis, as is shown in the upper half of the diagram. As changes in acid-base balance occur the balance of K, on a normal intake of this ion, becomes negative in amounts closely equal to the surplus losses of Cl. As K is lost in the urine and alkalosis progresses, the serum concentration of K falls. In the final three days of the study NH_4Cl was administered to repair the deficit of Cl and reversal of the changes in serum and balance take place. The gain of K during recovery is identical with losses of the initial periods and is carried out without the need for added K. The losses and gains of K are, at most, no more than 2 to 3

mEq./kg. body weight and can hardly be considered as significant deficits. We emphasize this point to indicate that deficit of K, in the sense of requiring replacement, is not always the basis for depressed serum K concentrations. Correction of the disturbance in acid base equilibrium is sufficient to allow correction of the negative balance of K in the presence of a normal intake. The occurrences just described are analagous to those occurring in patients with prolonged vomiting, with the exception that the latter group will almost always show some degree of dehydration and have had a deficient intake of K as well as other ions. The illustration just given should not be taken to indicate that

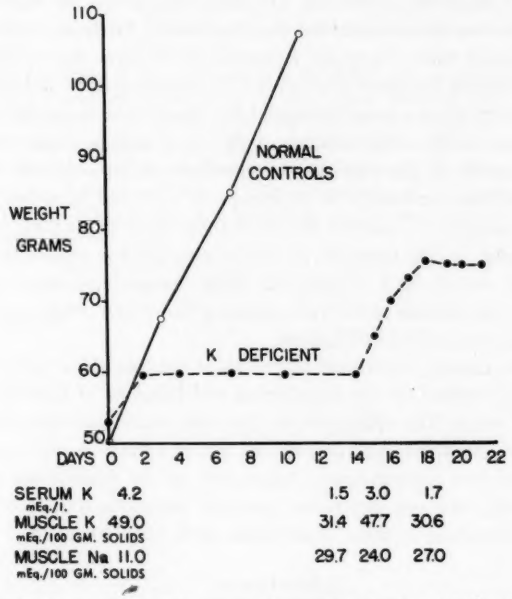


CHART 4. Relation of weight gain, serum K, muscle Na and K during development and repair of K deficiency in albino rats.

NH_4Cl will repair the deficits occurring in patients with prolonged vomiting: water, Na, K and Cl will all be ultimately necessary. The data do indicate that proper balance of K cannot occur in the presence of a disturbed acid-base equilibrium.

The equilibrium between intra- and extracellular K and Na has been termed "biological"[21] because of the relatively long periods of time required for their adjustment, unlike the nearly instantaneous ones that take place across semipermeable membranes such as the capillaries. Chart 4 is taken from data of Dr. Robert Schwartz in a study of the rate of repair of the muscle K deficit in depleted young growing rats. The composite rate of growth of the control animals is shown along the solid line. In the animals deprived of K, with a diet otherwise normal, growth stops after two days and weight remains stationary for the next 12 days. On the fifteenth day 25 mEq./kg. body weight of KCl was administered in an eight hour period. This quantity was chosen from data of previous experiments indicating that this represented the approximate deficit

present in the animals. An attempt at quick total repair was thus made. Resumption of weight gain, on the same deficient diet, was immediate and at the same rate as the controls. Repair allowed for persistence of weight gain during a four day period. Below the time ordinate are shown the serum and muscle analyses from groups of animals taken at intervals from the composite whole. On the day prior to repair the serum K concentration was low, muscle K was 60% of normal and muscle Na was nearly three times the normal. Twenty-four hours after repair muscle K was normal, muscle Na little changed and serum K concentration increased. Four days later muscle and serum had returned to their previous pattern of deficit. The administered K was diluted by the weight gain that it originally stimulated. The data indicate that the repair of intracellular K deficit is rapid when deficit exists but that the loss of Na from intracellular fluid is a relatively slow process when Na intake is normal. If the data shown here are applicable to the repair of clinical instances of K deficit, it would seem to indicate that repair of the intracellular losses alone cannot be dependably relied upon to quickly restore the extracellular fluid deficits of Na. The exchange of Na for K may be dependent upon separate mechanisms. The results of the experiments reported here are similar to those of Conway and Hingerty.[24] At this juncture it is of interest to note that K in equal quantities administered as the acetate, i.e., without the fixed anion chloride, is toxic for such depleted animals, death occurs in the majority. Cl seems essential for repair. In a similar series of experiments in which KCl 25mEq./kg. body weight was given in a four hour period, about half the animals died. This indicates that repair, while rapid, has a certain upper limit in time for its accomplishment.

To summarize in closing, we should like to point out that extra- and intracellular fluid are most accurately defined by the distribution and behavior of their respective electrolytes in the body water. The differences in the distribution and behavior of intra- and extracellular electrolyte allow for considerable independence in the regulation of acid-base balance of the two compartments. Adjustment of the equilibrium between the two phases is a relatively slow one dependent upon the metabolic activity of the cells. Some of the clinical implications of these observations have been discussed.

References

1. Muntwyler, E., Mellors, R. C., Mautz, F. R., and Mangun, G. H., Electrolyte and water exchange between tendon and blood, J. Biol. Chem. **134**:345, 1940.
2. Manery, J. F., Danielson, I. S., and Hastings, A. B., Connective tissue electrolytes, J. Biol. Chem. **124**:359, 1938.
3. Hastings, A. B., Electrolytes of tissues and body fluids, The Harvey Lectures, Series 35, 1940-41, pp. 91-125.
4. Shohl, A. T., Mineral Metabolism, American Chemical Society, New York City, Reinhold Publishing Corporation, Monograph 82, 1939.
5. Kruhöffer, P., Inulin as indicator for extracellular space, Acta physiol. Scandinav. **11**:16, 1946.
6. Nichols, N., and others, unpublished data.
7. Guest, G. M., and Rapoport, S., Role of acid soluble phosphorous compounds in red blood cells, Am. J. Dis. Child. **58**:1072, 1939.
8. Hastings, A. B., and Eichelberger, L., Exchange of salt and water between muscle and blood, J. Biol. Chem. **117**:73, 1937.
9. Gamble, J. L., Companionship of water and electrolytes in organization of body fluids, Lane Medical Lectures, Stanford, Calif., Stanford University Press, 1951.
10. Cotlove, E., Holliday, M. A., Schwartz, R., and Wallace, W. M., Effects of electrolyte depletion and acid-base disturbance on muscle cation, Am. J. Physiol., to be published.

11. Wallace, W. M., and Hastings, A. B., Distribution of bicarbonate ion in mammalian muscle, J. Biol. Chem. **144**:637, 1942.
12. Rosenbaum, J. D., Influence of alterations in acid-base balance upon transfers of carbon dioxide and bicarbonate in man, J. Clin. Investigation **21**:735, 1942.
13. Schwartz, R., and Wallace, W. M., unpublished data.
14. Kety, S. S., Polis, D. B., Nadler, C. S., and Schmidt, C. F., Blood flow and oxygen consumption of human brain in diabetic acidosis and coma, J. Clin. Investigation **27**:500, 1948.
15. Butler, A. M., and others, Metabolic studies in diabetic coma, Tr. Am. A. Physicans **60**:1, 1947.
16. Cotlove, E., unpublished data.
17. Fenn, W. O., Role of potassium in physiological processes, Physiol. Rev. **20**:377, 1940.
18. Overman, R. R., Sodium, potassium and chloride alterations in disease, Physiol. Rev. **31**:285, 1951.
19. Steinback, H. B., Intracellular inorganic ions and muscle action, Ann. New York Acad. Sc. **47**:849, 1947.
20. Buchanan, J. M., Hastings, A. B., and Nesbitt, F. B., Effect of ionic environment on synthesis of glycogen from glucose in rat liver slices, J. Biol. Chem. **180**:435, 1949.
21. Darrow, D. C., Schwartz, R., Iannucci, J. F., and Coville, F., Relation of serum bicarbonate concentration to muscle composition, J. Clin. Investigation **27**:74, 1948.
22. Elkinton, J. R., Winkler, A. W., and Danowski, T. S., Transfers of cell sodium and potassium in experimental and clinical conditions, J. Clin. Investigation **27**:74, 1948.
23. Schwartz, W. B., and Wallace, W. M., Electrolyte equilibrium during mercurial diuresis, J. Clin. Investigation **30**:1089, 1951.
24. Conway, E. J., and Hingerty, D., Relations between potassium and sodium levels in mammalian muscle and blood plasma, Biochem. J. **42**:372, 1948.

300 Longwood Avenue

ANOMALIES OF THE PULMONARY VEINS AND THEIR SURGICAL SIGNIFICANCE

Report of Three Cases of Total Anomalous Pulmonary Venous Return

By HARRY G. PARSONS, M.D., ANN PURDY, M.D., AND BRUCE JESSUP, M.D.
San Francisco

THE brilliant and epochal advances of the past decade in surgery of the heart and its great vessels have been concerned primarily with the correction of anomalies of the outflow tracts, namely, the aorta and pulmonary arteries. Careful study of the inflow tracts suggests the possibility of directing the surgeon's ingenuity into correcting the incapacitating abnormalities that occasionally involve the pulmonary veins.

Brody[1] in 1942 presented an excellent review and analysis of 106 reported cases of anomalies of the pulmonary veins. Since this review, 30 cases have been added by various authors,[2-15] bringing the total number to 136. In 55 cases, the pulmonary veins drained entirely into the right auricle or its tributaries, and in 81 cases this drainage was incomplete. Twenty cases of total drainage into the right auricle or its tributaries were associated with other major cardiac anomalies and 35 cases (table 1) were without such anomalies.

TABLE 1

TOTAL ANOMALOUS PULMONARY VENOUS DRAINAGE WITHOUT OTHER CARDIAC ANOMALIES

Into:	Cases
Superior vena cava	5
R auricle	5
L innominate vein	5
Coronary sinus	9
Inferior vena cava	1
Portal vein	3
Persistent L superior vena cava	5
Ductus venosus	2
Total	35

Cases of persistent left superior vena cava without other associated anomalies are usually asymptomatic and compatible with long life, as Papaez'[16] review of 200 cases indicates. The anomaly results from a persistence of the left precardinal veins.

Cases of persistent left superior vena cava into which both pulmonary veins empty are rare (Fig. 1). In such cases the aerated blood returning from the lungs passes successively into the persistent left superior vena cava, the left innominate vein, the superior vena cava, and thence into the right auricle. The pulmonary venous blood which has

From the Department of Surgery and Department of Pediatrics, Stanford University School of Medicine, San Francisco.

(Received for publication June 11, 1951.)

mixed with the peripheral venous blood may now take one of three routes: it may pass into the right ventricle, the pulmonary artery, the lungs and the pulmonary vein and again complete the vicious cycle; the mixed blood may pass into the right ventricle, the pulmonary artery and by way of the patent ductus arteriosus into the peripheral arterial system; or the mixed blood may pass through the patent foramen ovale, the only portal of entrance into the left auricle, thence to the left ventricle, and finally to the peripheral

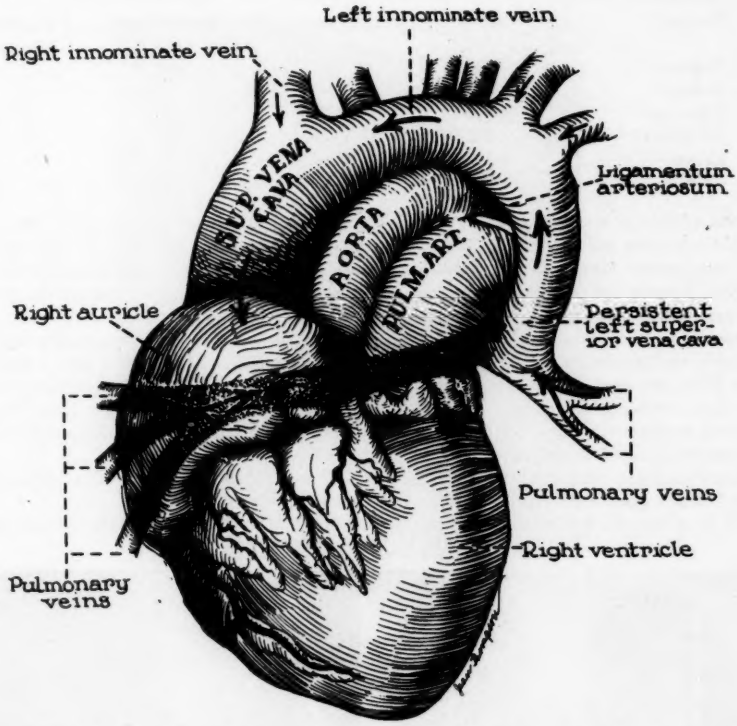


FIG. 1. Central defect consists of persistent left superior vena cava into which both pulmonary veins empty. There is also patent foramen ovale.

arterial system. Only six such cases have been reported in the literature[2, 11, 17–20] (table 2). The first case was reported by Turner in 1822 and was associated with other cardiac anomalies consisting of a single atrium and one functional ventricle. The remaining cases were not associated with other major cardiac anomalies.

This paper reports two cases of persistent left superior vena cava into which both pulmonary veins empty.

CASE REPORTS

Case 1: B.J.A.,* a female 3 yr. of age, was first seen in the Stanford Clinic, because of dyspnea and palpitation. Mother's pregnancy and the patient's development had been normal. Though believed not to be a "blue baby," she became cyanotic with crying, her breathing was rapid and her heart

* Referred by Dr. Norbert Frey, Nevada City, Nev.

TABLE 2

CASES OF PERSISTENT LEFT SUPERIOR VENA CAVA INTO WHICH ALL PULMONARY VEINS EMPTY

Author	Age at Death	Patent Ductus Arteriosus	Patent Foramen Ovale	Right Side Hypertrophy
Turner[20]	infant	?	Single atrium	1 functional ventricle
Epstein[13]	10 days	?	—	?
Chaffey[2]	11 wk.	—	—	—
Schroeder[19]	26 days	?	—	?
McManus[18]	12 mo.	—	—	—
Kernan[11]	4 mo.	—	—	—

beat was audible in a quiet room. She tired easily and voluntarily limited her activity. Her weight gain had been poor and she was small and pale with a slight cyanosis of the lips and nail beds. Neck veins were greatly distended and pulsated vigorously. Chest wall was markedly asymmetric with precordial bulging and pulsation. Heart rate and respirations were rapid. A loud systolic murmur with thrill maximum along the L sternal margin and at the apex was widely transmitted throughout the chest and upper abdomen. Liver was 2 fingerbreadths below the costal margin. She had been maintained on digitalis for 1 yr. by her family physician. RGs (Fig. 2) showed a huge round heart almost filling the chest. Pulmonary vascular tree was greatly enlarged. Two large pulsating shadows were found extending up and out from the hilar regions overshadowing the upper lung lobes and suggesting mediastinal masses. ECG showed a R axis deviation, biphasic QRS complexes and abnormal RST segments. Circulation time was 15 sec. by the fluorescine method.

Clinical diagnosis was indefinite until the publication of a similar case by Drs. Johnson and McRae,[10] who suggested the possibility of an anomaly of the venous return.

At 6 yr. of age, she was readmitted to the hospital for cardiac catheterization. The catheter entered

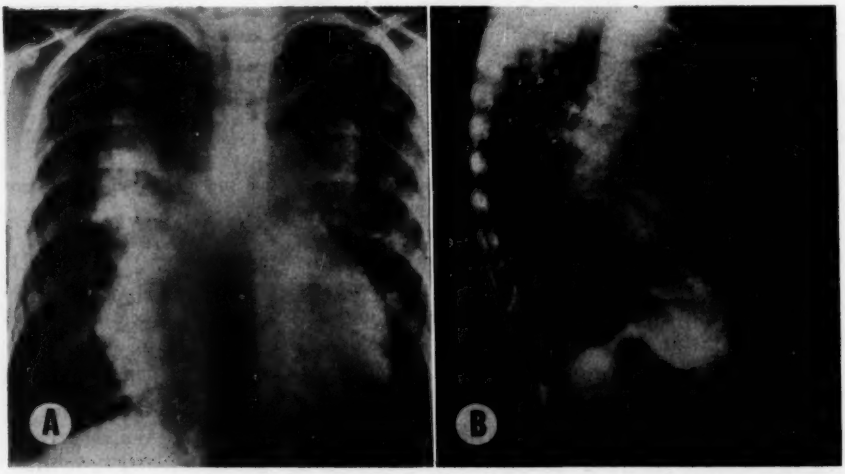


FIG. 2. A. Heart is massively enlarged both to R and to L. Two large areas of increased density are seen extending laterally from midline in supracardiac area. B. Heart is huge, filling most of chest. Note anterior bowing of sternum.

and coiled in the prominent mass on the R side of the mediastinum from which 98% oxygen-saturated blood was withdrawn. Pressures in the pulmonary artery (73/43) and right ventricle (81/41) were elevated. Blood samples from both the R auricle and the R ventricle showed a 95% oxygen-saturation. From these studies, it was concluded that the large mediastinal mass on the R side was a hugely dilated superior vena cava which received a large quantity of blood from the pulmonary veins. An auricular septal defect was also demonstrated by passing the catheter into the L auricle. It was concluded that the pulsating mass in the L upper mediastinum was probably a persistent L superior vena cava. A few hours after an uneventful catheterization, she died in pulmonary edema.

FIG. 3. Sternum has been removed and lungs and anterior thorax are being held back on both sides. Heart is markedly enlarged and fills almost ¾ of chest. Superior mediastinum is greatly widened by dilated anomalous venous channels.

Clinical Diagnosis:

1. Congenital cardiovascular disease.
   a. Double superior vena cava.
   b. Anomalous pulmonary venous return (pulmonary veins empty into R side of heart).
   c. Interauricular septal defect.
2. Chronic congestive heart failure.

Permission for autopsy was limited to the removal of the heart and lungs. Heart was huge and filled ¾ of the chest. Pleural cavities contained no fluid. Organs were in their normal relative positions. Liver was enlarged. Anomalous venous channels widened the anterior mediastinum to approximately 9 cm. (Fig. 3). The absence of the normal venous pulmonary attachment of the heart permitted its easy displacement. Right pulmonary vein ran to the base of the heart and joined with the L pulmonary vein directly behind the L auricle (Fig. 4). This common pulmonary venous trunk then ran upward through the L anterior mediastinum as a persistent L superior vena cava (20 mm. in diameter) and joined with the L subclavian vein and internal jugular vein at the level of the sternal notch (Fig. 5). Thence, it ran across the anterior superior mediastinum as a dilated L innominate vein to the R mediastinum where it joined with the R innominate vein to form a markedly dilated R superior vena cava (32 mm. in diameter).

Superior and inferior venae cavae entered a markedly hypertrophied and dilated R auricle in the normal manner (Fig. 6). Foramen ovale (12 mm. by 8 mm.) was anatomically patent. Right ven-

tricle was hypertrophied and dilated. Myocardium was 10 mm. thick and the papillary muscles were large. Left auricle was small and received no tributaries (Fig. 7). The only portal of entry to the L auricle was the foramen ovale. Mitral valve was normal. Left ventricular chamber was small and its myocardium measured 12 mm. There was no interventricular septal defect. The cardiac valves, especially the pulmonary and tricuspid, were diffusely thickened with moderate blunting of the edges, but there were no vegetations present. Tricuspid valve was 9 cm. in circumference, the pulmonary 5 cm., the mitral 6 cm. and the aortic valve 3.5 cm. Endocardium was normal throughout.

Pulmonary artery proximal to its bifurcation measured 2.2 cm. in diameter. Ascending aorta

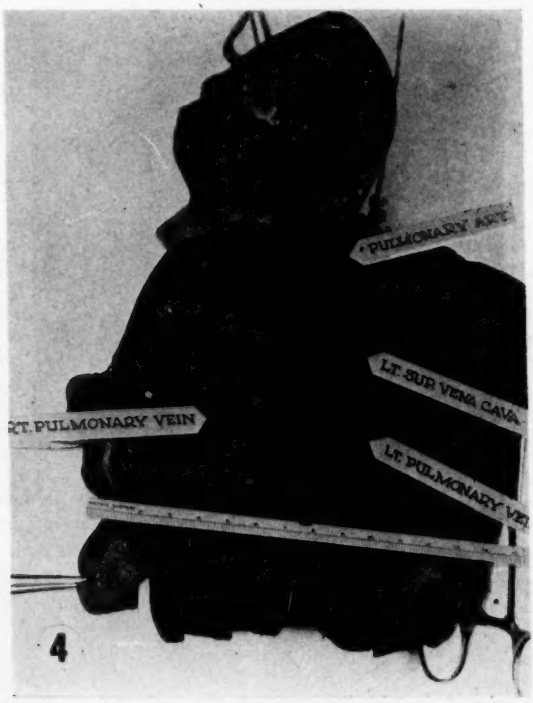


FIG. 4. Heart is turned back away from lungs. Primary abnormality consists of persistent L superior vena cava into which all pulmonary veins empty. Note groove in L upper lung as result of pressure from dilated persistent L superior vena cava.

measured 1.1 cm. in diameter. Ductus arteriosus was 4 mm. in diameter and 10 mm. long. It was not patent.

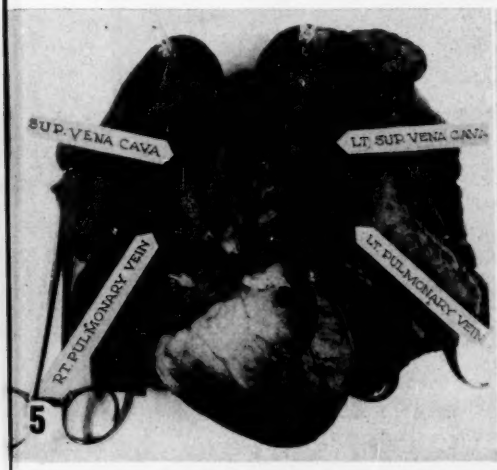
Lungs were edematous. Trachea contained considerable frothy, clear fluid and much of the same fluid exuded from the cut surface of the lung. There was no evidence of hyperemia, consolidation or infarction.

Microscopic Studies: Endocardium of the R ventricle was approximately 5 times as thick as that of the L ventricle. Muscle fibers of the R auricle and ventricle were hypertrophied and larger than those of the left. Cardiac valves, especially those of the R heart, all showed a diffuse thickening and increase of collagenous fibrous tissue. Numerous dilated blood vessels were seen throughout the lung sections. In some sections, large macrophages filled with brown granules (heart failure cells) were seen in the alveoli and septa. Sinusoids of the liver and spleen were distended with red blood cells. An occasional macrophage with brown granules was seen. No increase of fibrous tissue.

Pathologic Diagnosis:

1. Congenital cardiovascular malformation.
   a. Persistent L superior vena cava.
   b. Absence of pulmonary venous return to L auricle.
   c. Persistent foramen ovale.
   d. Fibroelastosis of tricuspid valve.
   e. Dilatation and hypertrophy of the R auricle and ventricle.
   f. Fibroelastosis of endocardium of R auricle and R ventricle.
2. Chronic congestive heart failure, mild.

Case 2, L.B., a female, was born of a pregnancy complicated by abdominal pain necessitating bed rest for the 1st 6 mo. Slight cyanosis was noted at birth. By the fifth day of life there was definite cyanosis. At 3 wk. a heart murmur was first heard and spells of dyspnea, choking and deep cyanosis occurred. When examined at 9 wk. of age, the child was noted to be well developed, fairly well



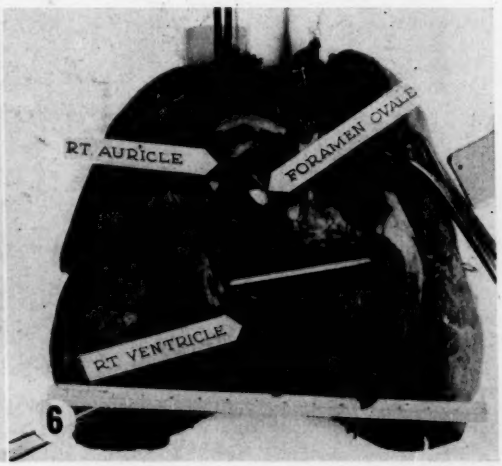


FIG. 5. L superior vena cava receives blood from both pulmonary veins and runs cephalad to join L subclavian and jugular veins to form transverse L innominate vein which empties into R superior vena cava. Note relative size of pulmonary artery and ascending aorta.

FIG. 6. R auricle and ventricle are greatly hypertrophied and dilated. Tricuspid valve is thickened and papillary processes are huge.

nourished and tachypneic. There was cyanosis of the entire body which did not appear to deepen with crying or increased activity. Heart was enlarged to percussion. There was no asymmetry of the chest. A loud systolic murmur without thrill was heard over the entire precordium, loudest over the base of the heart at the L sternal border. Fine scattered rales were heard throughout both lung fields. Liver was markedly enlarged and the tip of the spleen was easily palpated. There was mild edema present, particularly of the eyes and feet. Chest RGs (Fig. 8) showed cardiomegaly with large hilar shadows extending to both sides of the mediastinum at the base of the heart. Clinical diagnosis was cyanotic congenital heart disease, probably anomalous pulmonary venous return, with cardiac decompensation. The child was hospitalized, but died 9 hr. after admission.

Autopsy* showed the heart was enlarged. The pulmonary veins which drained the lobes of the R lung merged within the hilum into a single channel which passed anterior to the main stem

* The material was made available through the courtesy of Dr. Charles M. Blumenfeld, Sacramento, Calif.

bronchi, esophagus, and aorta, immediately below the bifurcation of the trachea. It then curved upward and joined the veins from the hilum of the L lung to form a single venous channel, a persistent L superior vena cava (Fig. 9A). Left superior vena cava joined a dilated venous channel occupying the position and general relations of the L innominate vein. The cut ends of the L subclavian and internal jugular veins were visible at the L upper border of the innominate vein. The dilated L innominate vein joined the R innominate vein to form a superior vena cava which emptied in a normal manner into the R atrium (Fig. 9B). Right atrium was markedly dilated with enlarged pectinate muscles, the walls averaging 1 mm. in thickness. The ostia of the coronary sinus and of the superior and inferior vena cavae were not remarkable. A large patent foramen ovale measured

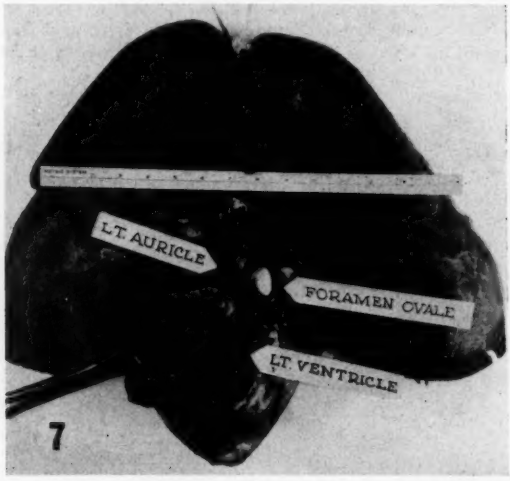


FIG. 7. L auricle and ventricle are small. All blood entering L side of heart must pass through large, patent foramen ovale.

1.8 cm. by 1.4 cm. Right atrioventricular orifice was moderately dilated. Tricuspid valve was normal in appearance. Right ventricle was notably dilated with walls averaging 4 to 5 mm. in thickness. Interventricular septum was intact. Left atrium was small and the walls averaged 1 mm. in thickness. No venous channels opened directly into the L atrium. Walls of the L ventricle measured 5 to 6 mm. in thickness. Aorta and aortic valve, the pulmonary artery and valve, and coronary orifices were normal. There was no trace of a ductus arteriosus.

Pathologic Diagnosis:

1. Congenital heart disease.
   a. Anomalous pulmonary venous return with drainage into a persistent L superior vena cava.
   b. Patent foramen ovale.
   c. Dilatation and hypertrophy of R auricle and ventricle.
2. Congestive heart failure.

The primary abnormality in these cases was a persistent left superior vena cava into which all the pulmonary veins emptied. The oxygenated blood was then carried to the right auricle by passing from the left superior vena cava into the left innominate vein, thence into the right superior vena cava. Much of the blood which entered the right ventricle completed this vicious cycle over and over again. The only blood reaching the left ventricle and arterial tree was that which entered the left auricle through the patent foramen ovale. In the first case, judging from the comparatively large size of the

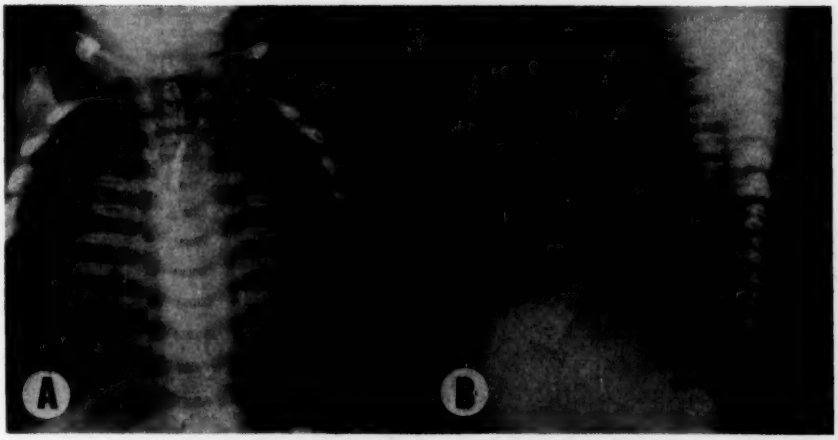


FIG. 8A and B. Heart is massively enlarged. Two large areas of increased density are seen extending laterally from midline in supracardiac area.

ligamentum arteriosum, it may have been open within the past year or two. The late closure of the patent ductus probably accounted for the change in her clinical course. In the second case, it would seem that with growth and increased activity, possible reduction in the size of the foramen ovale, and absence of a ductus arteriosus that progressive right heart strain and failure occurred.

Cases in which both pulmonary veins empty into the ductus venosus are rare (Fig. 10).

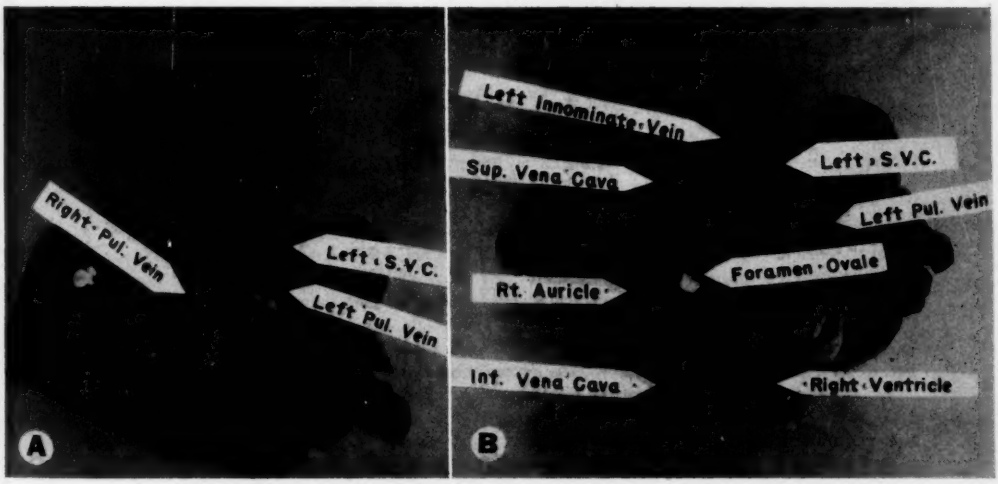


FIG. 9A. Heart is turned back away from lungs. All pulmonary veins empty into persistent L superior vena cava.

FIG. 9B. L superior vena cava runs cephalad to join L subclavian and jugular veins to form transverse L innominate vein which empties into R superior vena cava.

In these cases the aerated blood returning from the lungs passes successively into a common pulmonary vein that descends with the esophagus through the diaphragm and then the ductus venosus, the inferior vena cava, and thence into the right auricle. As shown with the first two cases the pulmonary venous blood which has mixed with the peripheral venous blood may now take one of three routes: It may pass into the right ventricle,

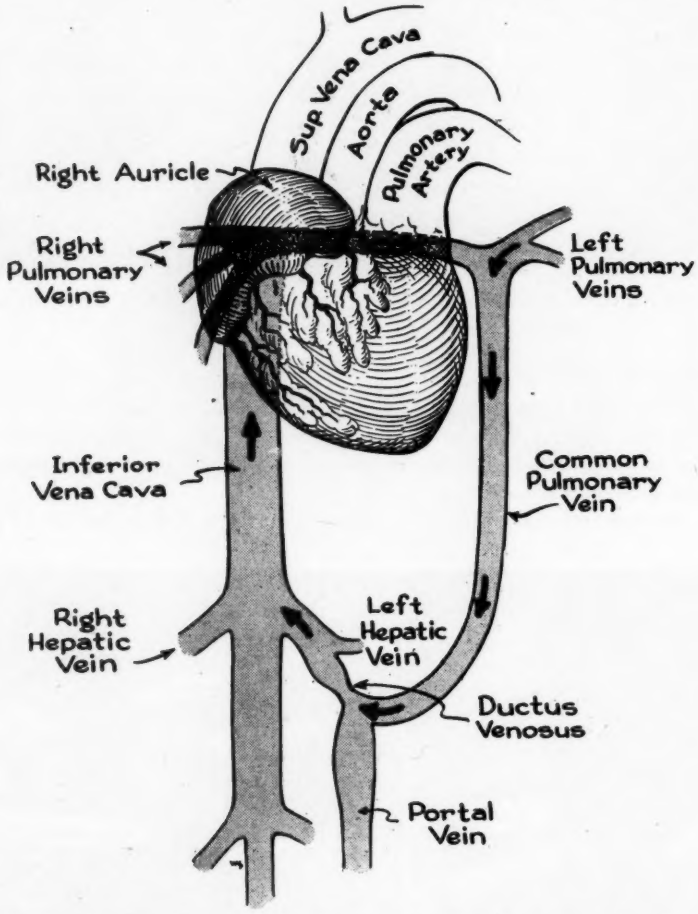


FIG. 10. Both pulmonary veins empty into ductus venosus through common pulmonary vein that descends through chest and diaphragm. There is also patent foramen ovale.

the pulmonary artery, the lungs, the pulmonary vein and again complete the vicious cycle; the mixed blood may pass into the right ventricle, the pulmonary artery and by way of the patent ductus arteriosus into the peripheral arterial system; or the mixed blood may pass through the patent foramen ovale, the only portal of entrance into the left auricle, thence to the left ventricle, and peripheral arterial system. Three such cases have been reported in the literature.[6, 21, 22] One of the three cases[22] had multiple cardiac anomalies consisting of an interventricular septal defect and coarctation of the aorta.

Case 3*: B. T., a female, was born of a mother who had been treated for syphilis with full doses of penicillin during the fourth month and again during the eighth month of her pregnancy. The child was born at term. The cord Wassermann was positive. Physical examination at birth and again on the fifth day of life was not remarkable. The mother noted on the seventh day that the baby, while attempting to pass a stool, suddenly became dyspneic and cyanotic. This condition persisted for 10 min. until a stool was passed and the dyspnea subsided. Similar attacks of dyspnea occurred regularly twice a day with each bowel movement. At 4 wk. the child had a severe attack of dyspnea and cyanosis and was taken to the San Francisco Hospital. Physical examination revealed a cyanotic

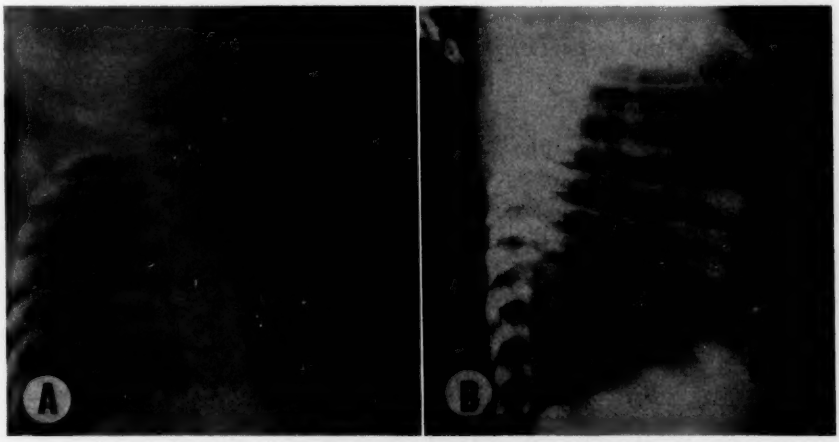


FIG. 11A and B. Heart and lungs are not remarkable.

child in great respiratory distress. Heart was not enlarged to percussion and there was no murmur or thrill. Percussion note over the thorax was hyperresonant and no rales were heard. Liver extended to the level of the umbilicus. RGs (Fig. 11A and B) were not remarkable. ECGs suggested R ventricle strain. Child was placed in oxygen on arrival and after 24 hr., respirations were neither labored nor rapid and cyanosis had disappeared. Forty-eight hours after entry, while straining to defecate, the child's respirations became labored and gasping, and there was deep cyanosis despite continuous oxygen. The infant died 30 min. later. Clinical differential diagnosis included: underlying pulmonary pathology to explain emphysema and R heart strain; anomalous L coronary artery; congenital myocardial fibroelastosis; cardiac glycogen storage disease; and anomalous pulmonary venous return.

Autopsy showed R auricular and ventricular enlargement. Liver was greatly enlarged. Pulmonary veins from each lung converged to form a common pulmonary venous trunk which did not enter the L atrium but without branching descended below the diaphragm to empty into the ductus venosus (Fig. 12a). The circumference of this pulmonary vessel was, at its widest point, 13 mm. The circumference of the ductus venosus at the site of junction with the common pulmonary vein was 5 mm. Portal vein was not unusual. Hepatic veins drained normally into the inferior vena cava which entered the greatly dilated R auricle in the usual manner (Fig. 12b). Foramen ovale was widely patent and its orifice measured 10 mm. by 12 mm. Right ventricular wall was 6 mm. thick. Interventricular septum was intact. Tiny L auricle received blood only through the foramen ovale. Heart valves, pulmonary artery, aorta and coronary vessels were not remarkable. Ductus arteriosus measured 11 mm. in length and admitted a fine probe. Lungs were meaty red, firm and dry. Trachea and major bronchi were normal in appearance and free of fluid.

---

* The material was made available through the courtesy of the Public Health Department, San Francisco County Hospital and Dr. Eileen Harrington, Assistant Resident, Pathology, San Francisco County Hospital.

Pathologic Diagnosis:

1. Congenital heart disease.
   a. Anomalous total pulmonary venous drainage into the ductus venosus.
   b. Right auricular and ventricular hypertrophy.
   c. Patent foramen ovale.

The third case presents an almost identical anomaly as was seen in the case reported by Edwards and DuShane.[6] The aerated blood from the lungs emptied into the narrow ductus venosus from which it either passed directly into the inferior vena cava or refluxed into the portal system and then passed through the liver sinusoids, hepatic veins, and thence to the inferior vena cava. The mixed blood then reached the systemic circulation

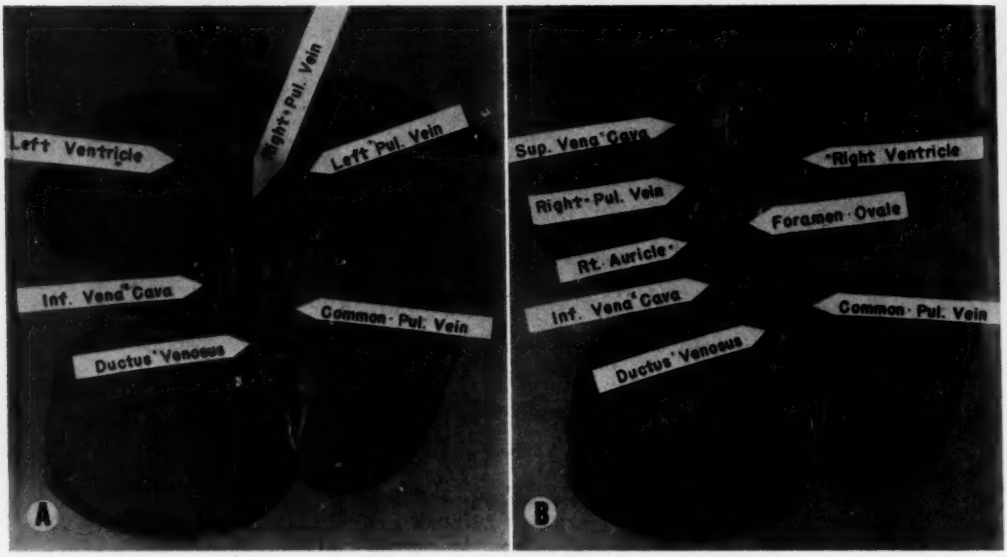


FIG. 12A. Pulmonary veins from each lung converge to form common pulmonary vein which descends in chest, through diaphragm, and enters liver to empty into ductus venosus.
FIG. 12B. Ductus venosus drains into inferior vena cava which enters R auricle in normal manner. Foramen ovale is widely patent.

by passing through the patent foramen ovale into the left auricle, left ventricle and aorta. It was pointed out by Edwards and DuShane that in this anomaly the narrowness of the ductus venosus constitutes a barrier to pulmonary venous return. In the patient reported here the clinical importance of this barrier was observed. Straining at stool resulted in increased intrathoracic and intra-abdominal pressures which produced dyspnea, tachypnea and cyanosis. With the increased intrathoracic and intra-abdominal pressures, there resulted a constriction of the long, thinned walled common pulmonary vein.

Ziegler[15] recently reported a case of a 4 year old girl in which a diagnosis of total pulmonary venous drainage into the superior vena cava was made by clinical and cardiac catheterization studies and confirmed by autopsy. The patient died on the second day following thoracotomy for the attempted surgical relief of her condition. A similar case of a 2 year old boy with total pulmonary venous drainage into the left innominate vein was reported by Friedlich, Bing and Blount.[7] The diagnosis was based on clinical and cardiac

catheterization studies and confirmed by autopsy following death several hours after operation. These two cases and the case of Drs. Johnson and McRae are, as far as is known, the first cases diagnosed in life.

Taussig[13] states that the diagnosis is based upon finding great enlargement of the right side of the heart combined with little or no cyanosis. Cardiac arrhythmia or paroxysmal tachycardia also may be present. Progressive cardiac enlargement and right-sided heart failure are the rule. The diagnosis is definitely established by catheterization of the right auricle and by comparing the oxygen saturation of the blood in the right auricle with that of the arterial blood. This is the only malformation in which the two values can be both high and almost identical. A persistent left superior vena cava can be differentiated from the other anomalies in which both right and left pulmonary veins empty into the right side of the heart by the demonstration of the pulsating left superior mediastinal mass.

The exact origin and mode of development of the pulmonary veins has never been conclusively established.[23-32] Investigators agree the venous pulmonary tree arises from a capillary plexus, derived from the general splanchic plexus, which communicates freely with the cardinal system of veins. Anomalous pulmonary veins always drain into some structure originating from the vitalline or cardinal veins.

It is reasonable to expect that in the future a greater number of malformations of the pulmonary veins will be diagnosed during life. The increased use of angiograms and cardiac catheterization coupled with a growing interest in cardiovascular anomalies will make this possible. As the various anomalies of the pulmonary veins are more widely known, they will be recognized more frequently at the operating table. The anomalies in which there is incomplete drainage of the pulmonary veins into the right side of the heart are rarely diagnosed prior to death. When only one or two of the pulmonary veins open into the right auricle and the remainder of the pulmonary veins open in the normal manner into the left auricle, the course of the circulation is not altered seriously enough to produce a clinical picture that can be diagnosed during life. The lives of such patients are usually normal and not shortened by the anomaly.

Brantigan[33] pointed out the importance of detecting anomalous pulmonary veins at the time of lobectomy. If the pulmonary vein of the upper lobe drained into a tributary of the right side of the heart, and if the pulmonary vein of the lower lobe drained normally into the left auricle, then removal of the lower lobe would result in a greater amount of pulmonary venous blood being returned to the right side of the heart. This would increase the strain on the heart. On the other hand, if the upper lobe was removed it would eliminate the return of oxygenated blood to the right heart and would be beneficial to the patient. The most common anomalous pulmonary venous drainage is the drainage of the pulmonary vein of the right upper lobe of the lung to the superior vena cava.

Brantigan[33] and Taussig[13] have suggested that when it is possible to diagnose during life cases of complete anomalous pulmonary venous return to the right side of the heart, it should be possible to treat them surgically by anastomosing a major pulmonary vein to the left auricle. On the basis of his analysis of all the cases in the literature of incomplete anomalous drainage of the pulmonary veins into the right auricle or its tributaries, Brody[1] concluded that when less than 50% of the pulmonary venous blood is returned to the right heart, there is little likelihood of decompensation.

It would appear that the treatment of choice is to anastomose one of the main pulmonary venous trunks to the left auricle or auricular appendage. This could be accomplished, and still allow 50% of the pulmonary venous blood to continue its course

unobstructed while the anastomosis is being made. This is probably all the blood the small left side of the heart could tolerate at one time. However, if the patient is still not sufficiently improved, the remaining main pulmonary venous trunk can be anastomosed to the left auricle or its appendage, after a long enough period of time has elapsed to allow the left heart to adjust itself to the first increase in its load. Gerbode[34, 35] in the laboratory has worked out the operative technic and has demonstrated in dogs the feasibility of anastomosing large veins to either the right or left auricular appendages and to the atrium.

Conclusion

Some hope may be offered to the patient with complete anomalous drainage of the pulmonary venous system. The diagnostic tools are at hand and the method of anastomosing large veins to the auricular appendages has been developed in the laboratory. But it still remains for the clinician to make the diagnosis and for the surgeon to apply the known and established principles for the correction of the first case of total anomalous pulmonary drainage to the right side of the heart.

Summary

The successful operations upon abnormalities of the outflow tracts of the heart suggest that surgical measures may also be applied to the correction of abnormal inflow tracts.

Technically the anastomosis of veins to the auricle has been proved feasible in the experimental animal. Therefore, it should be possible to correct abnormally placed pulmonary veins in man.

A wide variety of such anomalies occur. In 55 of 136 reported cases, all the oxygenated blood from the lungs was returned to the right heart through anomalous vessels. Thirty-five per cent of these cases of complete diversion were accompanied by other major cardiac defects. It is estimated that 50% or more of the return flow from the lungs must reach the right heart to produce clinical symptoms.

Two cases are presented of persistence of the left superior vena cava which transmitted all the freshly oxygenated blood to the right auricle, by way of the left innominate and the right superior vena cava.

The clinical picture was that of growth retardation, minimal cyanosis, a huge hyperactive heart, a loud left mesocardial systolic murmur, pulsating shadows in both upper pulmonary fields, and nearly identical oxygen-saturation of blood obtained from the right heart and femoral artery.

One case is reported in which all the oxygenated blood from the lungs is carried to the right auricle by way of the ductus venosus.

Surgical correction of the abnormality of these cases by transplantation of one or more of the veins would have been possible. However, no case known to the authors has yet been successfully corrected.

References

1. Brody, H., Drainage of pulmonary veins into right side of heart, Arch. Path. **33**:221, 1942.
2. Chaffey, W. C., Malformation of pulmonary veins, Tr. Path. Soc. London **36**:183, 1885.
3. Compere, D. E., and Forsyth, H. F., Anomalous pulmonary veins: Report of case, J. Thoracic Surg. **13**:63, 1944.
4. Conant, J. S., and Kurland, L. T., Pulmonary tuberculosis associated with anomalous common left pulmonary vein entering left innominate vein, J. Thoracic Surg. **16**:422, 1947.
5. Duff, P. A., Pulmonary veins from both lungs draining into right auricle with persistent foramen ovale: Report of case, J. Tech. Methods **18**:106, 1938.

6. Edwards, J. E., and DuShane, J. W., Thoracic venous anomalies, Arch. Path. **49**:517, 1950.
7. Friedlich, A., Bing, R. S., and Blount, S. G., Jr., Physiological studies in congenital heart disease, Bull. Johns Hopkins Hosp. **86**:20, 1950.
8. Gotman, D. W., and Stern, N. S., Congenital heart disease, Am. Heart J. **18**:176, 1939.
9. Hughes, C. W., and Rumore, P. C., Anomalous pulmonary veins, Arch. Path. **37**:364, 1944.
10. Johnson, A., and McRae, D., Combined use of angiocardiograms and cardiac catheterization in diagnosis of congenital anomalies of cardiovascular system, PEDIATRICS **2**:643, 1948.
11. Kernan, J. D., Obstruction of right main bronchus due to congenital maldevelopment of pulmonary veins, Ann. Otol. **53**:818, 1944.
12. Sanes, S., Anomalous drainage of pulmonary veins into coronary sinus, Am. J. Dis. Child. **58**: 354, 1939.
13. Taussig, Helen B., Congenital Malformations of Heart, New York, Commonwealth Fund, 1947, p. 309.
14. Young, M. O., Common trunk of pulmonary veins tributary to portal vein with multiple cardiac anomaly, Arch. Path. **44**:169, 1947.
15. Ziegler, R. F., to be published.
16. Papaez, J. W., Two cases of persistent left superior vena cava in man, Anat. Rec. **70**:191, 1938.
17. Epstein, A., Transposition der Aorta und Pulmonalarterie ohne Septum-defect: Persistenz des Isthmus aortae und des Ductus Arteriosus, Ztschr. f. Heilkunde **7**:308, 1886.
18. McManus, J. F. A., Case in which both pulmonary veins emptied into persistent left superior vena cava, Canad. M. A. J. **45**:261, 1941.
19. Schröder, R., Über Anomalien der Pulmonalvenen, zugleich ein Beitrag zum Cor biloculare, Virchows Arch. f. path. Anat. **205**:122, 1911.
20. Turner, in Discussion of case of congenitally malformed heart, Lancet **2**:1034, 1882.
21. Ghon, A., Ein Beitrag zu den Anomalien der Pulmonalvenen, Beitr. z. Path. u. z. allg. Path. **62**:175, 1916.
22. Mehn, W. H., and Hirsch, F. E., Drainage of pulmonary veins into ductus venosus arantii, Am. J. Path. **23**:125, 1947.
23. Brown, A. J., Development of pulmonary veins in domestic cat, Anat. Rec. **7**:299, 1913.
24. Buell, C. E., Jr., Origin of pulmonary vessels in chick, J. Contrib. Embryol. **14**:11, 1922.
25. Chang, Chun, On origin of pulmonary vein, Anat. Rec. **50**:1, 1931.
26. Davies, F., and MacConaill, N. A., Cor biloculare with note on development of pulmonary veins, J. Anat. **71**:437, 1937.
27. Fedorow, V., Über die Entwickelung der Lungenvene, Anat. Hefte **1**:122, 1910.
28. Flint, J. M., Development of lungs, Am. J. Anat. **6**:1, 1906-1907.
29. Goette, A., Die Entwickelungsgeschichte der Unke (bombinator igneus) als Grundlage einer vergleichenden Morphologie der Wirbeltiere, Leipzig, 1875.
30. Keith, A., Human Embryology and Morphology, ed. 5, Baltimore, William Wood & Company, 1933, p. 36.
31. Mollendorf, W., Über Anlage und Ausbildung des Kiemenlungenkreislaufs bei Anuren (bombinator pachypus), Anat. Hefte **141**:249,1912.
32. Patten, B. M., Human Embryology, Philadelphia, The Blakiston Company, 1946, p. 644.
33. Brantigan, O. C., Anomalies of pulmonary veins: Their surgical significance, Surg., Gynec. & Obst. **84**:653, 1947.
34. Gerbode, F., Yee, J., and Rundle, F. F., Experimental anastomosis of vessels to heart, Surgery **25**:556, 1949.
35. Gerbode, F., and Hultgren, H., Observations on experimental arteriovenous anastomosis with particular reference to congenital anomalies of venous return to heart and to cyanosis, Surgery **28**:235, 1950.

SPANISH ABSTRACT

Anomalías de las Venas Pulmonares y su Significancia Quirurgica; Reporte de Tres Casos con Anomalías Totales de las Venas Pulmonares

Los brillantes descubrimientos de los últimos díez años en la cirugía de el corazón y los grandes vasos se concentraron primariamente en la corrección de las anomalías de la aorta y arterias pulmonares. Sin embargo, el estudio cuidadoso de las vías de la circulación de retorno sugiere la posibilidad de

dirigir la ingenuidad de los cirujanos hacia la corrección de las anomalías que ocasionalmente afectan las venas pulmonares.

Ciento treinta y seís casos de anomalías de las venas pulmonares han sido reportados en la literatura, notandose que en 55 de estos casos toda la sangre oxigenada de los pulmones fué retornada a la auricula derecha o sus tributarios.

Tres casos de anomalías totales de las venas pulmonares han sido estudiados recientemente. La anormalidad primaria en dos de los casos fué la persistencia de una vena cava superior izquierda en la cual desembocaban todas las venas pulmonares. La sangre oxigenada fué transportada hacia la auricula derecha mediante el pasaje de la sangre de la vena cava superior izquierda a la vena innominada izquierda, y de aqui la vena cava superior derecha. La mayor parte de la sangre que entraba en el ventriculo derecho completaba este circulo vicioso que continuaba repitiendose. La única sangre que llegaba al ventriculo izquierdo y circulación arterial fué aquella que procedia de la auricula izquierda via foramen ovale. El conducto arterioso estaba cerrado. El cuadro clinico se caracterizó por la presencia de retardo del crecimiento, cianosis mínina, hipertrofia marcada del corazón, soplo sístolico mesocardico izquierdo, contracciones de las sombras radiograficas de ambos campos pulmonares superiores, y saturación de oxigeno casí idéntica de la sangre obtenida de la arteria femoral y del corazón derecho.

En el tercer caso toda la sangre oxigenada de los pulmones desembocaba en el conducto venoso, de el cual la sangre podía pasar directamente a la vena cava inferior o mediante su reflujo en la circulación portal pasar atráves de los sinusoides del higado, venas hepaticas y de aquí a la vena cava inferior. Esta sangre así mezclada alcanzaba la circulación general vía foramen ovale, auricula izquierda, ventriculo izquierdo y finalmente arteria aorta.

La corrección quirurgica de las anormalidades de estos casos mediante la transplatación de una o más de las venas pulmonares hacia la auricula o tributarios auriculares hubiera sido posible.

Clay and Webster Streets

PAROXYSMAL TACHYCARDIA IN INFANTS AND CHILDREN

Study of 41 Cases

By ALEXANDER S. NADAS, M.D., C. WILLIAM DAESCHNER, M.D., ARTHUR ROTH, M.D., AND STANLEY L. BLUMENTHAL, M.D.
Boston

PAROXYSMAL rapid heart action was first described by Stokes in 1854.[1] It was not until 1889 that Bouveret[2] called it essential paroxysmal tachycardia and described a patient in whom "Each paroxysm begins and ends suddenly, in a few seconds." Ashman and Hull[3] describe the mechanism as a "usurpation" of the normal S-A nodal rhythm by some ectopic focus or circuit due to the more rapid discharge of impulses by the latter. This mechanism is similarly considered by Katz.[4]

Ectopic rhythms may be divided into supraventricular and ventricular types contingent upon their origin above or below the A-V node. Levine[5] described a bedside differentiation of these varieties, but observers rely on the electrocardiogram for the classification of the arrhythmia. The width and shape of the ventricular complexes form the basis of differentiation of the two types. The QRS complexes in supraventricular tachycardia are "usually of normal outline and similar to those present during normal rhythm in a given case."[6] In ventricular tachycardia "the ventricular complexes are of abnormal outline and quite unlike those present during normal rhythm."[7] Under certain circumstances, these criteria do not hold and one must identify the exact P-QRS relationship in order to classify the arrhythmia. However the P-waves may be either of low voltage or superimposed on the preceding T-wave.

The cardiac rates in paroxysmal tachycardia may vary from 140 to over 300/min. and may last from a few seconds to several days or longer.

The clinical picture, prognosis and treatment of paroxysmal tachycardia in adults has been the subject of many excellent reports based on large series of carefully studied cases.[8–12] Since the first description of paroxysmal tachycardia in an infant,[13] over 150 cases of the disease in the pediatric age group have been described. Hubbard[14] reported the largest series—nine cases. Others[15–19] have reported more than one patient.

The present report is based on 41 patients studied within the past 20 years at the Children's Hospital of Boston and includes the nine cases previously reported from this institution by Hubbard.[14] The authors hope to present a clinical and electrocardiographic pattern characteristic of paroxysmal tachycardia in infants and children and to indicate therapy and prognosis.

I. CLINICAL FEATURES

Etiology: An analysis of the possible etiologic factors is given in table 1. Etiologic factors were not revealed in 24 cases. However, five cases of the Wolff-Parkinson-White

From the Sharon Cardiovascular Unit and the Children's and Infants' Hospital of the Children's Medical Center, and from the Department of Pediatrics, Harvard Medical School, Boston.
Presented in part before the New England Cardiovascular Society, April 1951.
(Received for publication Aug. 20, 1951.)

syndrome (short P-R interval and abnormal QRS complexes) were in this group. Patients showing this syndrome at normal rates are prone to have attacks of paroxysmal tachycardia.[20]

The remaining 17 cases had a variety of diseases that may have been a factor in the causation of the tachycardia. There were four patients with infection and two patients whose only episodes of tachycardia occurred in association with anesthesia. In one of these two, preanesthetic administration of atropine sulfate was the predisposing factor. Eight patients had congenital heart disease. One patient's paroxysmal tachycardia began

TABLE 1

ETIOLOGIC CLASSIFICATION

Unknown			24
WPW		5	
Normal egg		19	
Known			17
Infection		4	
Anesthesia		2	
Congenital heart disease			
Unknown	4		
Tetralogy of Fallot	1		
Coarctation	1		
Ebstein's	1		
Ductus	1	8	
Skull fracture		1	
S–A node tumors		2	
Total			41

at the time of a skull fracture and has persisted to date. This case has been reported.[21] Two patients, at postmortem examination, were found to have a thickening of the tissue at the caval-auricular junction and these were interpreted as hamartomas of the S-A node. Both these patients died of unrelated causes and an S-A node tumor was not diagnosed during life.

Age at Onset: Age distribution is shown in chart 1. The majority occurred within the first four months of life and the other cases were scattered evenly over the remainder of childhood. The higher incidence of the disease in the first four months of life is also shown in chart 2.

If the presence or absence of probable etiologic factors with the two age groups is correlated in chart 3, it becomes obvious that the majority of the young infants showed no etiologic factors. In contrast, more than half the older children had diseases that may explain the tachycardia. The difference demonstrated in chart 3 is of probable statistical significance ($\chi = .07$).

Sex: Thirty-one patients were males. This male predominance has been observed by others.[10, 12] A hitherto unobserved and more striking relationship between sex and paroxysmal tachycardia is revealed if we correlate the sex incidence with the etiologic factors (chart 4). All but one of the patients with idiopathic disease were males. The

one female was a one day old baby. Among the group with known etiology, males and females are equally represented (χ less than .01). This difference is statistically highly significant.

Thus, based on age, sex, and the presence or absence of an etiologic factor, the cases

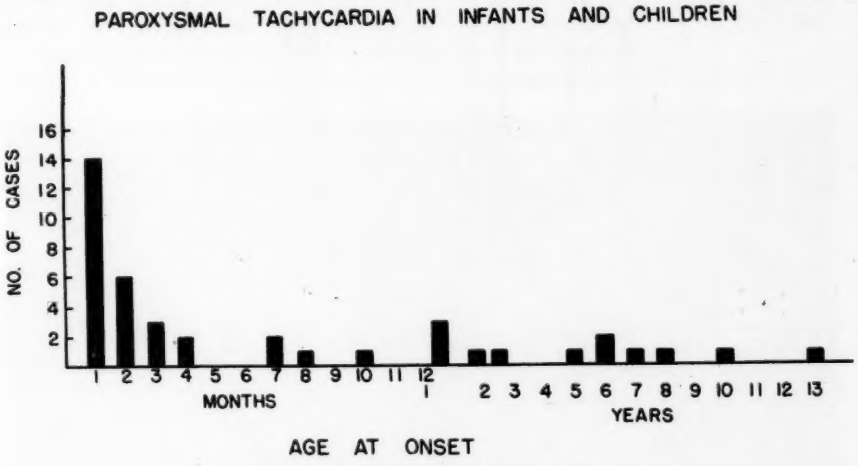


CHART 1. Distribution of patients by age at onset of disease. Note large number within 1st 4 mo. of life.

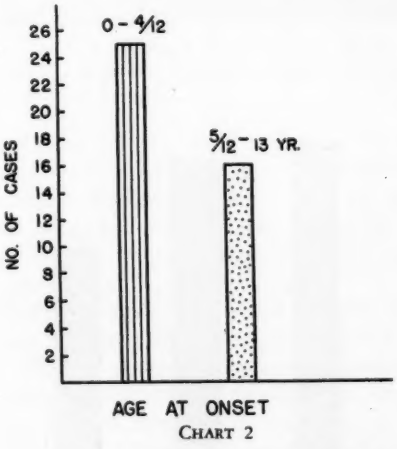


CHART 2

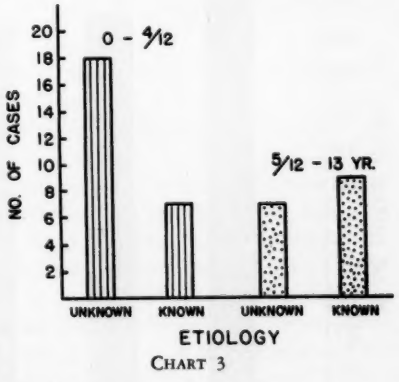


CHART 3

CHART 2. Size of young infant group (25) contrasted with size of group consisting of older infants and children (16).
CHART 3. Etiology in relation to age at onset.

divide themselves into two groups, one consisting of male infants less than 4 months of age without concomitant disease, the other of older children of either sex who may or may not have demonstrable etiology for the tachycardia.

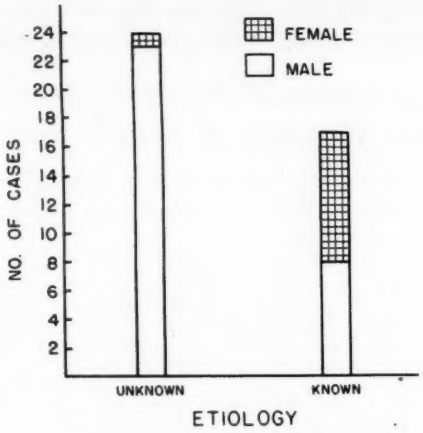


CHART 4. Sex in relation to etiology.

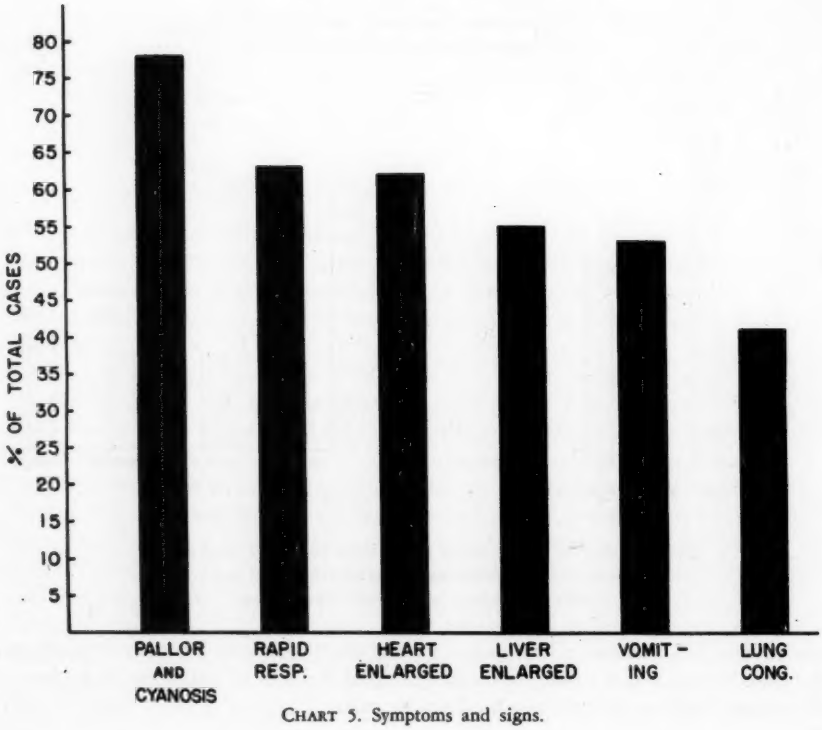


CHART 5. Symptoms and signs.

Symptoms and Signs: Seven of the 41 patients had paroxysmal tachycardia during a routine physical examination and had no symptoms. The majority of patients, especially the group of young infants with idiopathic paroxysmal tachycardia, were very ill patients. The color was often ashen gray. The skin was cold and wet with perspiration. They were restless and irritable. Respirations were rapid and labored. Often a hacking cough was present. The abdomen was distended. The picture resembled closely a severe pneumonia or septicemia; the excessively rapid cardiac rate led to the diagnosis.

Chart 5 tabulates the relative incidence of the symptoms and signs. In addition to either

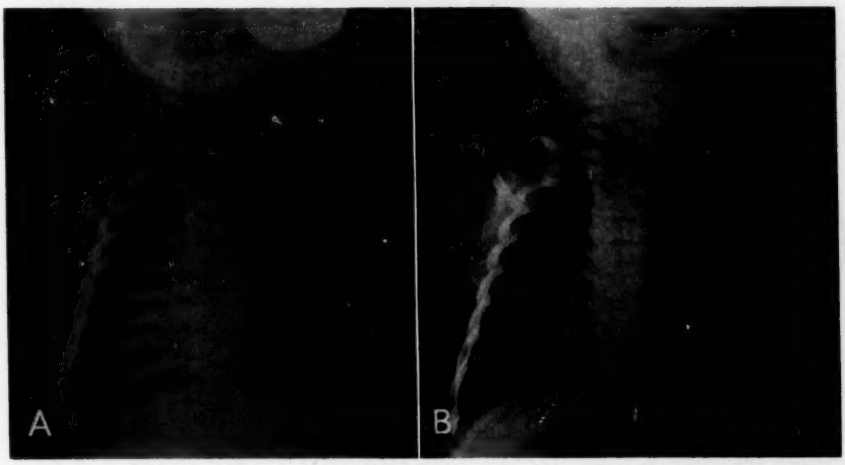


FIG. 1. A. During tachycardia. Note cardiac enlargement and pulmonary vascular congestion. B. Fourteen days after cessation of tachycardia. Note diminution in size of heart and disappearance of pulmonary congestion.

pallor or cyanosis, rapid respiration, enlargement of the heart and liver, vomiting, and pulmonary congestion were the most common manifestation.

Other findings, not included in the graph, were irritability, excessive perspiration, oliguria, peripheral edema and rales in the chest.

Seven of the patients had fever. Four of these had infections which might have caused the pyrexia. In the remaining three congestive failure was present. In all these, the elevated temperature returned to normal in a few hours after cessation of the attack without the use of chemotherapy. Fever is known to result from congestive failure alone.[14]

Systolic cardiac murmurs were present in 17 of the patients. In eight of these, the murmur persisted after the attack and was of Grade III intensity or more. These patients were found later to have congenital heart disease. In nine patients, the murmur was transient, of Grade I-II intensity, and was probably caused by the combination of rapid cardiac rate and cardiomegaly. Diastolic murmurs were not observed in this series.

Wolff[8,9] has stated that palpitation and precordial pain are among the cardinal symptoms of paroxysmal tachycardia in adults, and that congestive failure almost never occurs. In contrast to this congestive failure is the most important single finding in the paroxysmal tachycardia of infants and children, while pain and palpitation were not noted.

Laboratory: The laboratory studies usually revealed normal findings. Urine examina-

tions were consistently negative as were blood studies except that of 13 cases in which a white blood cell count above 15 thousand/cmm. was recorded. Five of these patients had an associated infection, six had elevated white blood cell counts associated with cardiac failure without evidence of infection. In two cases, the leucocytosis could not be explained.

Roentgenography: Evidence of cardiac enlargement and pulmonary vascular congestion were present in all patients with congestive cardiac failure. In a number of children in whom clinical evidence of failure was equivocal, the roentgenogram showed evidence of cardiac enlargement. The enlargement usually involved both ventricles and was described as "non-specific in contour." Atrial enlargement was commonly demonstrated by posterior displacement of the barium-filled esophagus. It was possible to observe the patterns of improvement in the roentgenographic findings after cessation of the paroxysmal

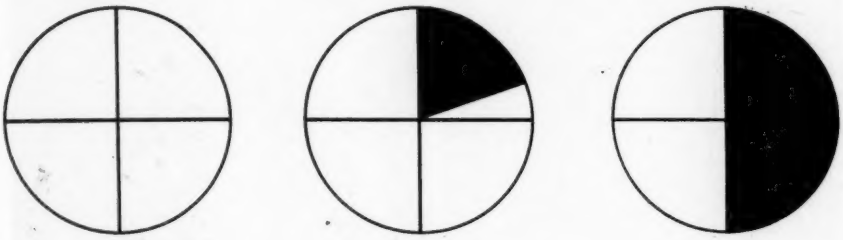


CHART 6. Duration of tachycardia and development of congestive failure. (C.F. = congestive failure.)

tachycardia (Fig. 1). In general, the lungs cleared in from 48 to 72 hours, and the heart began to decrease in size within 36 hours but frequently did not return to normal completely for 10 to 14 days.

Cardiac Failure: Most of the signs and symptoms of paroxysmal tachycardia in infants and children are explained by the presence of cardiac failure. We have accepted, as criteria for this, enlargement of the liver, peripheral edema, pulmonary congestion, and reversible cardiomegaly. Slightly better than half the patients (22 cases) showed evidence of failure.

The presence or absence of congenital heart disease did not seem to be a determining factor in the development of failure since five of the patients with congenital heart disease showed failure and three did not.

The cardiac rate influenced the development of congestive failure only insofar as none of the patients with rates below 180/min. developed failure. There were only four patients in this category, all over 5 years of age. Among the majority of patients showing a rate of 180 to 330/min. (37 cases), the degree of tachycardia did not seem to influence the development of failure since half the patients with failure showed rates between 180 and 240 min. and an equal number ranged between 250 and 330/min.

The duration of the tachycardia seemed to be a significant factor in the production of failure. None of the patients whose attack lasted 24 hours or less went into failure (chart 6). One fifth of those whose episodes lasted 36 hours and half of those whose paroxysms lasted 48 hours showed evidence of failure.

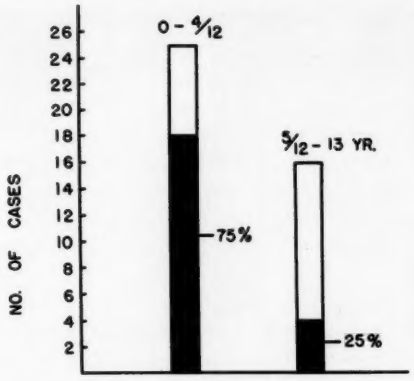


CHART 7. Incidence of congestive failure in 2 age groups

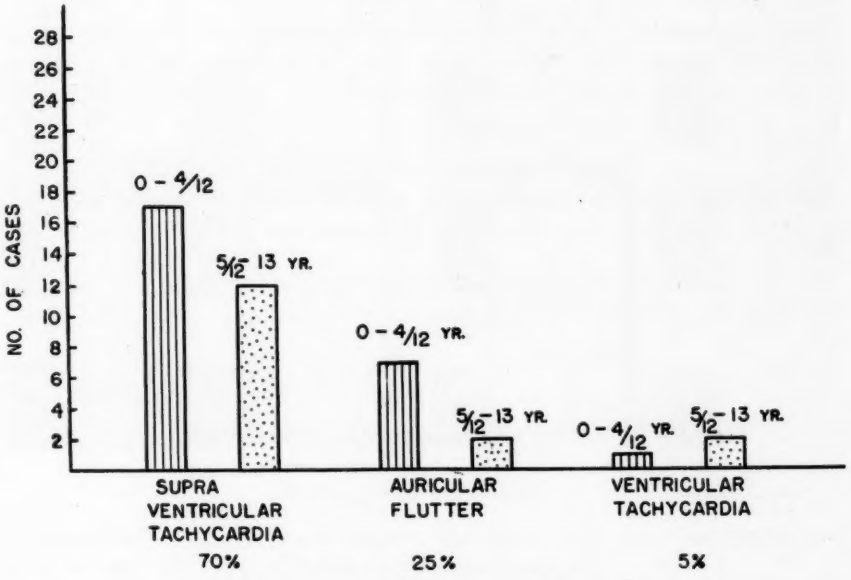


CHART 8. Type of tachycardia and age at onset.

If the cases with cardiac failure are considered according to age (chart 7), the majority of the young age group showed failure with paroxysmal tachycardia whereas only a minority of the older children developed it.

Since the overwhelming majority of young patients show rates over 180/min. during paroxysms, the deciding factor at these rates is the duration of the tachycardia and the age of the patient. It can be assumed that the young infant develops failure because he is unable to call attention to his tachycardia and it is not recognized by the parents and treated by a physician until the manifestations of cardiac failure appear.

II. Electrocardiograms

Electrocardiograms were available in 39 out of the 41 cases. The interpretation of other observers was used in the other two. Chart 8 illustrates the incidence of the various types of paroxysmal tachycardia in the two age groups. It can be seen that 70% of the patients had supraventricular tachycardia; 25% had auricular flutter; and only 5% showed ventricular tachycardia. There seemed to be no significant correlation between the age of the patient and the type of tachycardia except for the rarity of ventricular tachycardia in the younger age group. This observation is based on only three cases but is supported by other reports in the literature.[22] Figures 2, 3 and 4 show ECGs representative of the three types of tachycardia.

Analysis of Tracings During Paroxysm: The rates varied from 160 to 330/min. The mean rate was 240/min. with a standard deviation of the mean of plus or minus 49.

P-waves were identifiable in only three instances. In all the cases designated as auricular flutter, f-waves could be demonstrated in at least two limb leads, mostly Leads II and III (Fig. 3).

P-R intervals in the three patients whose P-waves were identified ranged from 0.08 to 0.13 sec.

QRS complexes in all cases of supraventricular tachycardia and flutter were similar to the ventricular complexes between attacks. Their duration ranged from .04 to .06 sec. An exception to this is the tracing from one patient with Wolff-Parkinson-White syndrome whose ventricular complexes were of bizarre outline and long duration (up to 0.12 sec.) both during and between attacks (Fig. 5). These probably represent supraventricular complexes with aberrant intraventricular conduction.

All the QRS complexes in the cases of ventricular tachycardia were by definition bizarre and wide (0.09 to 0.12 sec.) and unlike the complexes seen between attacks (Fig. 4).

T-waves were not distinguishable usually from the P-waves. Where they could be seen, they were usually inverted or diphasic in one or more of the standard limb leads.

Fig. 2. Supraventricular tachycardia. Standard limb leads I-III.

A. During attack
Rate 250/min.
P-R ?
QRS 0.05 sec.
QT ?
Note absence of P-waves, inverted T 3.

B. Between attacks
Rate 110/min.
P-R 0.11 sec.
QRS 0.05 sec.
QT 0.26 sec.
Note well outlined P 1-2. T 3 still inverted.

Fig. 3. Auricular flutter. Standard limb leads I-III.

A. During attack
Rate 300/min.
P-R ?
QRS 0.05 sec.
QT ?
Note 1:1 flutter.

B. Between attacks
Rate 145/min.
P-R 0.09 sec.
QRS 0.075 sec.
QT 0.26 sec.
Note short P-R interval, relatively wide QRS complex, ? WPW syndrome. P2 is more than 4 mm. tall. (P-wave only 2 mm. tall 1 wk. later.)

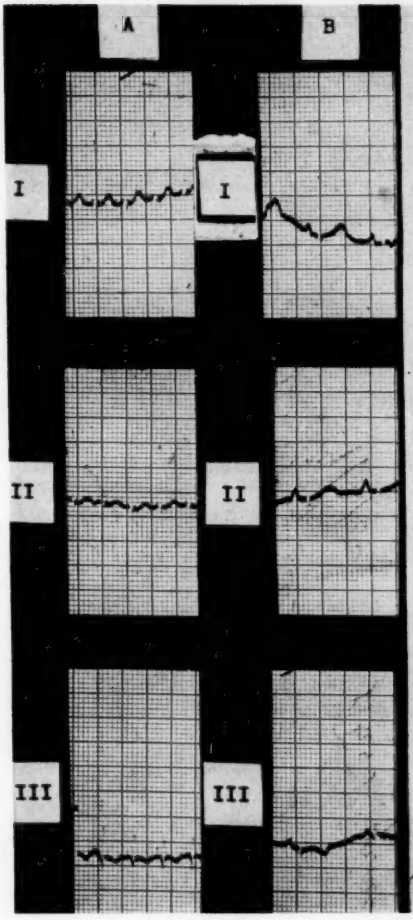


FIG. 2

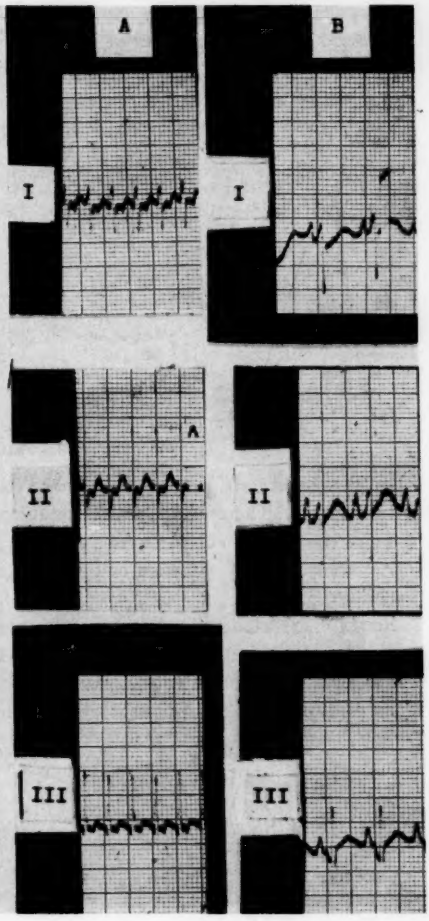


FIG. 3

For legends see opposite page.

Analysis of Tracings Between Paroxysms: The rates between attacks were comparable to those found in a group of normal children of similar age.

P-waves were commonly found to be tall and pointed immediately after resumption of normal rhythm. P_2 was 2.5 mm. or more in height in 10 cases.

P-R intervals were less than 0.10 sec. in nine instances. Five of these patients had the W-P-W syndrome; the others had normal ventricular complexes. Levine[23] recently suggested that patients showing short P-R intervals without the abnormal QRS complexes are prone to develop paroxysmal tachycardia.

QRS complexes were of average duration, with the exception of the cases with W-P-W syndrome in which the QRS interval was abnormally prolonged.

T-waves were diphasic or inverted in Leads I and II immediately after cessation of the

paroxysms in eight instances but returned to normal in a few days. S-T segments were depressed in an equal number of cases.

A summary of electrocardiographic findings is presented in table 2.

TABLE 2

SUMMARY OF ELECTROCARDIOGRAPHIC FINDINGS

	Rate		P Wave	P-R Interval		QRS Complex	S-T Segment	T-Wave
	Mean	S.D.		Mean	S.D.			
During Paroxysms	240	±49	Not visible	—	—	.04–.06 (except VT+WPW)	—	—
Between Paroxysms	122	±26	Present, often tall	0.108	±0.22	.04–.06 (except WPW)	Often depressed	Often depressed

S.D. = Standard deviation.

III. TREATMENT

In this series, six patients were observed whose paroxysmal tachycardia terminated spontaneously. There were several additional instances where the parents had noted spontaneous cessation of paroxysms at home.

A variety of methods were employed in an effort to terminate the tachycardia in the remaining 35 cases.

Reflex vagal stimulation by means of unilateral carotid sinus pressure, eyeball pressure, and induced vomiting was tried in at least 17 cases, with only one success. This patient was a boy 7 years of age with supraventricular tachycardia. Bilateral simultaneous carotid sinus pressure—a maneuver widely condemned—was attempted in one instance and was

FIG. 4. Ventricular tachycardia. Standard limb leads I-III.

A. During attack
Rate 180/min.
No constant P-R relation
QRS 0.08 sec.
QT ?
Note wide bizarre QRS complexes.

B. Between attacks
Rate 82/min.
P-R 0.16
QRS 0.05
QT 0.43 (upper normal at this rate .374)
Note definite P-R relationship, narrow QRS complexes and long QT interval. Latter is probably due to quinidine.

FIG. 5. Wolff-Parkinson-White syndrome with aberrant intraventricular conduction during and between attacks.

A. During attack
Rate 190/min.
P-R ?
QRS 0.11 sec.
QT ?
Note wide bizarre QRS complexes.

B. Between attacks
Rate 80/min.
P-R 0.07
QRS 0.16
QT ?
Note short P-R interval; wide bizarre QRS complex.

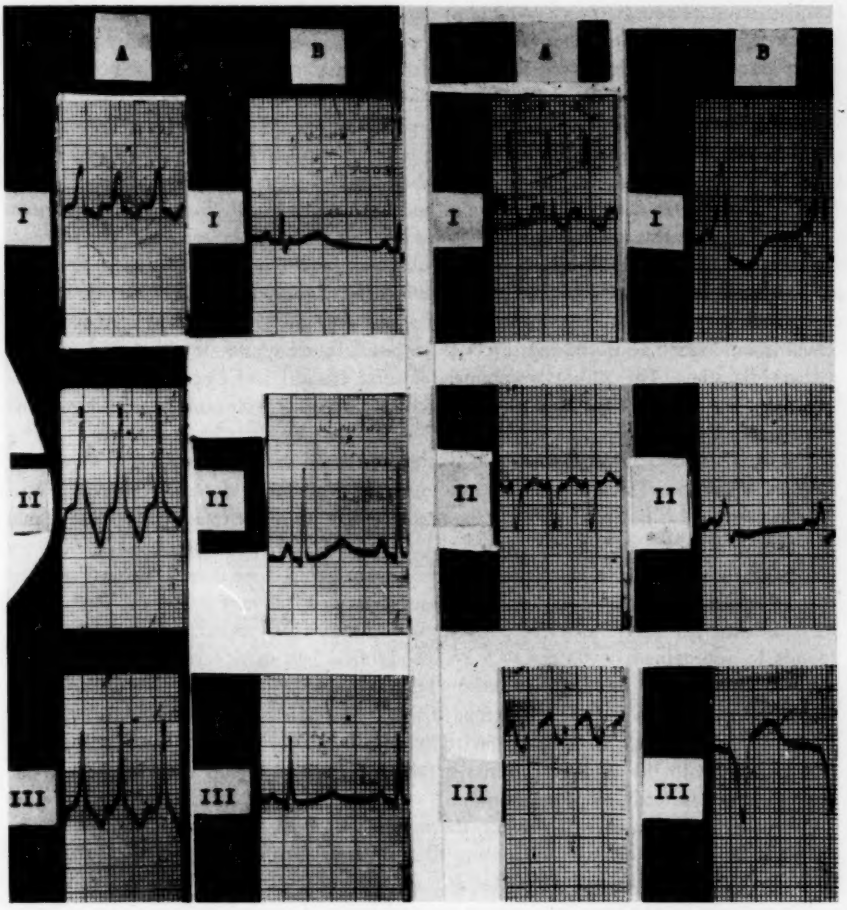


FIG. 4

FIG. 5

For legends see opposite page.

followed in 10 minutes by cardiac standstill and death. Whether the asystole was due to this maximal stimulation of the vagus nerve or to an overdose of digitalis is difficult to determine.

Prostigmin®* was tried in four patients with success in one. This one was a 12 year old girl with the W-P-W syndrome. The dosage of prostigmin® was calculated by weight on the basis of an adult dose of 0.5 to 1.0 mg.

Mecholyl®† was tried without success in five patients. One died within five minutes in

---

* Hoffman La-Roche

† Merck & Company, Inc.

cardiac arrest after intramuscular administration of the drug. One of the remaining four developed transient cardiac arrest, which responded to intravenous atropine. In the other three patients, there was clinical evidence of parasympathetic stimulation, but the paroxysm was not terminated. Because of this unfortunate experience with mecholyl®, its use is not recommended.

Quinidine was used in seven patients and restored normal rhythm in five. Two of these patients had ventricular tachycardia and the others had supraventricular tachycardia. All these patients were older children. Quinidine has been the first choice in the treatment of ventricular tachycardia in preference to procaine amide, largely because of more familiarity with the former drug.

The dosage of quinidine must be determined by clinical trial. After the absence of unfavorable side effects is demonstrated by a test dose of 25 to 50 mg. by mouth, the usual dosage schedule is 100 mg. every three hours by mouth for five doses or until the tachycardia stops. The authors recommend careful clinical and electrocardiographic observation of the patient for toxic effects which may necessitate termination of the planned program earlier.

Digitalis was administered to almost all the patients in varying doses and with varying degrees of success. The authors have examined the digitalizing doses of different preparations used in this institution during the past two decades in the treatment of paroxysmal supraventricular tachycardia and paroxysmal auricular flutter. The doses thus found were converted into equivalents of digitalis nativelle. Analyzing these data, it became obvious that all successfully treated patients (27 cases) received 1.0 to 1.2 mg. of digitoxin or its equivalent per square meter of body surface in a 24 hour period. This amount corresponds to approximately .03 mg./0.5 kg. in children less than 2 years of age and .02 mg./0.5 kg. in older children. The authors believe this to be the optimal digitalizing dose in the treatment of these patients. Except in the gravest of emergencies, it is preferable to administer this amount in three divided doses within 16 to 24 hours. One patient, a 12 year old girl with the W-P-W syndrome, failed to respond to this dosage schedule but responded satisfactorily to prostigmin®.

After conversion to normal rhythm, the majority of these patients were given a daily maintenance dose of digitalis amounting to approximately one-tenth of the digitalizing dose. This schedule was maintained for at least one week, sometimes considerably longer.

The digitalis preparations used within the past few years were largely digitalis nativelle intravenously or by mouth and digitalis lanata intravenously.

Oxygen was an important adjunct to therapy in all cases and was used throughout the period of tachycardia and until failure had cleared.

Antibiotics also played a significant role, mainly as prophylactic agents, in the acutely ill patient where the clinical differentiation of pneumonitis and pulmonary congestion could not be readily made.

Morphine sulfate in doses of 1 mg./4.5 kg. was administered to a few patients with marked effect on restlessness and irritability.

On the basis of this experience then, digitalis should be given an adequate trial in every case of supraventricular tachycardia and auricular flutter. If this proves ineffective, an unlikely event indeed, prostigmin® intramuscularly should be considered. In the therapy of ventricular tachycardia, this limited experience points to quinidine as the drug of choice, though the new procaine derivatives may well assume an equal role in the future.

It should be emphasized that these infants look desperately ill when first seen. The

physician's first inclination is to act at once and by heroic means to revert the rhythm to normal. In the authors' experience, conservative use of reliable drugs through a period of 12 to 24 hours is greatly preferable to administration of immediately acting but potentially dangerous therapeutic agents.

Prevention of Recurrences: Most of the patients, as has been said previously, were given medication for at least a week after cessation of their attack. Thirteen out of the group were given quinidine or digitalis for periods longer than a week in order to prevent further paroxysms. Data based on this group is not conclusive. The impression is, however, that the group with W-P-W syndrome and ventricular tachycardia has less frequent attacks if put on maintenance doses of quinidine. Whether the patient with paroxysmal auricular flutter and paroxysmal supraventricular tachycardia (without the W-P-W syndrome) has fewer attacks when on a maintenance dose of digitalis or quinidine is hard to evalute. The authors feel that it may be worth a trial without definite expectation of success.

IV. Prognosis

Complete follow-up data on 36 of the 41 patients is shown in table 3.

TABLE 3

Prognosis of Paroxysmal Tachycardia in 36 Patients

Death during attack		3
Following mecholyl therapy	1	
Following twice calculated digitalis dose and bilateral carotid sinus pressure	1	
Following cerebral embolism	1	
Death unrelated to tachycardia		2
Congenital heart disease and cardiac failure	1	
Cirrhosis of liver	1	
Surviving		31
Without recurrences	8	
1 to 3 recurrences	10	
Many recurrences	13	

Three patients died during one of their attacks; one following intramuscular mecholyl administration, another one following twice the calculated digitalizing dose and bilateral carotid sinus pressure. A third patient died in another hospital and autopsy revealed cardiac failure and cerebral embolism due to mural thrombi in the ventricles.

Two patients died from causes unrelated to their tachycardia; one in cardiac failure based on severe congenital heart disease; the other from cirrhosis of the liver.

Thirty-one patients were followed for periods varying from 1 to 20 years. Eight of them had no attacks beyond the initial one, 10 children had a few episodes and 13 patients had innumerable recurrences. The patients with W-P-W syndrome had more recurrences than those without this entity.

Relating the prognosis to the age at onset, in chart 9 we find that the young infant group does not tend to have recurrences beyond one year after the initial episode. The older children on the other hand show a pronounced tendency to recurrences beyond the first year after onset.

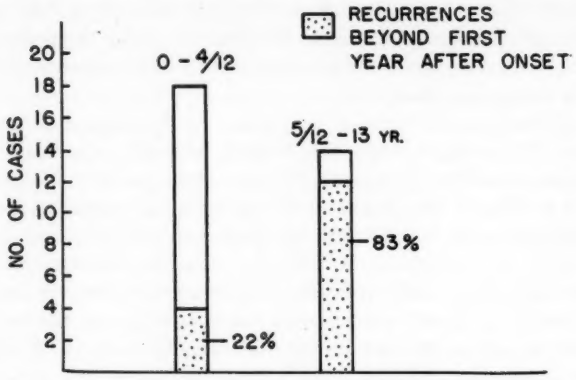


CHART 9. Recurrences of tachycardia in relation to age at onset in 32 cases followed for more than 1 yr.

SUMMARY

Forty-one cases of paroxysmal tachycardia in infants and children were studied. Male infants under four months of age with idiopathic tachycardia seem to represent a separate group among these children and can be contrasted with the group of patients over four months of age where males and females with tachycardia of known or unknown etiology are equally represented.

Congestive failure develops in the majority of the young infants with paroxysmal tachycardia but only in a minority of the older children.

Two factors which have a bearing on the development of congestive failure are duration of tachycardia at rates more than 180/min. and the age of the patient.

Twenty-nine patients showed electrocardiographic characteristics of supraventricular tachycardia; nine children had paroxysmal auricular flutter; three showed ventricular tachycardia.

The recommended drug for termination of supraventricular tachycardia and auricular flutter is digitalis nativelle or its equivalent. The optimal digitalizing dose corresponds to 1.0 to 1.2 mg./M^2 of body surface or .02 to .03 mg./0.5 kg. body weight. This amount should be administered in 12 to 24 hours. Ventricular tachycardia, it was found, responds well to quinidine.

As a maintenance dose for supraventricular tachycardia and auricular flutter, the authors recommend one-tenth of the digitalizing dose daily for at least one week, possibly longer. Quinidine is probably useful in preventing recurrences of ventricular tachycardia and of the tachycardias of the Wolff-Parkinson-White syndrome.

The prognosis for life is good. Recurrences within the first year are likely; beyond that period, only the older children and those representing the Wolff-Parkinson-White syndrome have further attacks.

ACKNOWLEDGMENT

The authors are indebted to Dr. Louis Wolff and Dr. Samuel A. Levine for their helpful criticism and to Dr. Jane Worcester for reviewing the data from a statistical viewpoint.

REFERENCES

1. Stokes, W., Diseases of Heart and Aorta, Dublin, Hodges & Smith, 1854, p. 161, cited in

Major, R. H., Classic Descriptions of Disease, Springfield, Ill., Charles C Thomas, Publisher, 1932, p. 366.
2. Bouveret, L., Concerning essential paroxysmal tachycardia, Rev. de méd. **9**:753, 1889, cited in Major,[1] p. 401.
3. Ashman, R., and Hull, E., Essentials of Electrocardiography, ed. 2, New York, The Macmillan Company, 1941, p. 214.
4. Katz, L. N., Electrocardiography, ed. 2, Philadelphia, Lea & Febiger, 1946, p. 624.
5. Levine, S. A., and Harvey, W. P., Clinical Auscultation of Heart, Philadelphia, W. B. Saunders Company, 1949, p. 72.
6. Rosenbaum, F. F., Clinical Electrocardiography, New York, Oxford University Press, 1950, p. 370 (51).
7. Rosenbaum,[6] p. 370 (52-53).
8. Wolff, L., Cardinal manifestations of paroxysmal tachycardia: Anginal pains, New England J. Med. **232**:491, 1945.
9. Wolff, L., Cardinal manifestations of paroxysmal tachycardia: Vascular collapse, New England J. Med. **232**:527, 1945.
10. Campbell, M., Paroxysmal tachycardias, Lancet **2**:641 and 681, 1947.
11. Cooke, W. T., and White, P. D., Prognosis of paroxysmal tachycardia and paroxysmal auricular fibrillation, Brit. Heart J. **4**:153, 1942.
12. Armbrust, C. A., Jr., and Levine, S. A., Paroxysmal ventricular tachycardia: Study of one hundred and seven cases, Circulation **1**:28, 1950.
13. Buckland, F. O., Case of rapid heart, Tr. Clin. Soc. London **25**:92, 1892.
14. Hubbard, J. P., Paroxysmal tachycardia and its treatment in young infants, Am. J. Dis. Child. **61**:687, 1941.
15. Neubauer, C., Paroxysmal tachycardia in infancy and childhood, Brit. Heart J. **7**:907, 1945.
16. Landtmann, B., Heart arrythmias in children, Acta pediat. (supp. 1) **34**:1, 1947.
17. Lyons, J. A., Excessively rapid heart rates: Report of case with autopsy, J. A. M. A. **108**:1393, 1937.
18. Taran, L. M., and Jennings, K. G., Paroxysmal atrioventricular nodal tachycardia in newborn infant, Am. J. Dis. Child. **54**:557, 1937.
19. Koplik, H., Paroxysmal tachycardia in childhood, Am. J. M. Sc. **154**:834, 1917.
20. Wolff, L., Parkinson, J., and White, P. D., Bundle branch block with short P-R interval in healthy young people prone to paroxysmal tachycardia, Am. Heart J. **5**:685, 1930.
21. Nadas, A. S., Alimurung, M. M., and Linenthal, A. J., Persistent ventricular pacemaker following basal skull fracture, Am. Heart J., to be published.
22. Rosenbaum, F. F., Johnston, F. D., and Keller, A. P., Paroxysmal ventricular tachycardia in childhood, Am. J. Dis. **64**:130, 1942.
23. Lown, B., Ganong, F., and Levine, S. A., Syndrome of Short P-R Interval, Normal QRS Complex and Paroxysmal Tachycardia, read by title at the Annual Meeting of the American Heart Association, Atlantic City, June 1951.

SPANISH ABSTRACT

Taquicardia Paroxistica en Infantes y Niños; Estudio de 41 Casos

Los autores revisan 41 casos de taquicardia paroxistica observados durante los últimos veinte años en el Children's Hospital de Boston.

De el estudio detallado de estos casos, es aparente la presencia de una entidad clinica dentro del grupo general de pacientes. Esta entidad consiste de un grupo de niños menores de cuatro meses de edad los cuales tienen tendencia a desarrollar insuficiencia cardiaca y a sufrir de ataques repetidos de taquicardia durant el primer año de la vida, pero en los cuales la ocurrencia de paroxismos al año después del primer ataque es extremadamente infrecuente.

El desarrollo de la insuficiencia cardiaca en este grupo de niños está relacionada con la duración mas prolongada de la taquicardia en comparación a los niños de mayor edad.

La mayoria de niños de este grupo carecian de enfermedad organica cardiaca acompañando la taquicardia.

La administración de digitalis a dósis relativamente grandes es el tratamiento indicado en estos casos.

300 Longwood Ave.

COAGULATION STUDIES IN THE NEWBORN INFANT

I. Normal Infants

By Burton J. Grossman, M.D., Ruth M. Heyn, M.D., and
Irving H. Rozenfeld, M.D.
Chicago

ALTHOUGH coagulation in the normal newborn infant has been studied by a number of investigators, these studies have usually been undertaken to establish the normal for a particular phase of the coagulation mechanism. Few studies have been done which correlate the multiple technics which are involved in the study of coagulation of whole blood.

This study was undertaken to furnish control data on a group of normal infants using technics which were also applied to the investigation of clotting in erythroblastosis fetalis. The studies include determinations of the whole blood clotting time, prothrombin time, protamine titration, heparin sensitivity, platelet counts, and gross observation for clot lysis in the same infant at the same time.

One of the earliest attempts to measure the whole blood clotting time in the newborn infant was the study by Rodda[1] in 1920, using a capillary blood technic. Others have subsequently reported normals for this age group using a capillary tube method or a plasma clotting technic. Lucas,[2] using the Lee-White method, reports a normal range of from 9 to 16 minutes.

Platelet counts have been done in the newborn period by Sanford,[3,4] Lucas[2] and Bray.[5] These counts have been within normal limits, as compared with adult values for similar technics and range from 190,000 to 350,000 platelets/cmm. of blood.

The various results obtained for prothrombin levels in the newborn are shown graphically in chart 1, which is taken from Grossman.[6] Although these represent the use of several methods of determination, it can be seen that the most significant variations occur in the first three days of life, and that prothrombin concentration approaches normal by the fifth day.

Protamine titrations, heparin sensitivities and gross observation of clot lysis have not been determined previously in the newborn period.

Methods

Determinations of whole blood clotting time, prothrombin time, protamine titration, platelet count and gross observation of clot lysis were done in 21 clinically normal newborn infants within 6 hr. of birth and again on the 3rd and 5th days of life. All these babies weighed more than 2500 gm.

These same determinations with the addition of the heparin sensitivity of the whole blood were done in 35 additional infants. A group of 5 infants was studied on each of the 1st 7 days of life.

Whole blood clotting time was done by the Allen modification[7] of the Lee-White method. The normal for this method in adults is 25 to 35 min. However the present authors used 0.5 cc. of blood in each tube instead of the 1.0 cc. used by Allen.

Platelet counts were done by the method described by Kristensen.[8]

Prothrombin times were determined using the one stage method of Quick.[9] However, with each series of prothrombin determinations, a control determination on a normal adult was obtained.

Department of Pediatrics, Bobs Roberts Memorial Hospital and Chicago Lying-in Hospital, University of Chicago School of Medicine, Chicago.

(Received for publication July 10, 1951.)

Protamine titration was measured by a modification of Allen's method,[10] using half amounts of heparin and blood. The normal adult value is 120 μg. of protamine. A normal control was done with each series of determinations. An increase of 20 or more μg. is considered a significant variation. This test determines the amount of protamine necessary to clot 1 cc. of standardly heparinized blood. It has been reported that patients with bleeding from various causes show an increase in the protamine titration, and that the bleeding stopped when the protamine titration was returned to normal by the use of protamine sulfate or toluidine blue.[11,12]

Heparin sensitivity was measured by the method described by Waugh and Ruddick.[13] This method measures the response of the whole blood clotting time to various dilutions of heparin. The sensitivity

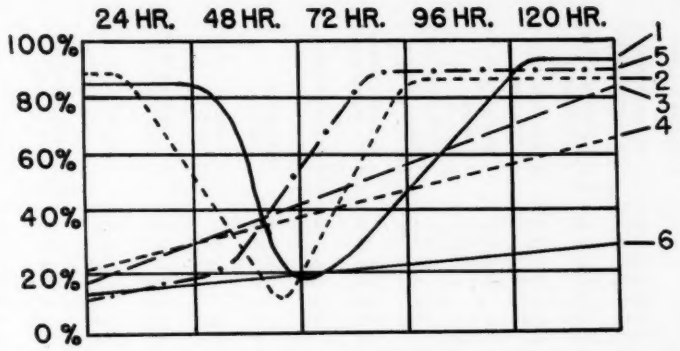


CHART 1. Comparison of prothrombin levels in newborn infant, according to various investigators: 1. Quick and Grossman, Waddell and Guerry, Smith and associates, Dam and Plum, MacPherson; 2. Nygaard; 3. Hellman and Shettles; 4. Poncher and Kato; 5. Kove and Siegel; 6. Smith, Warner and Brinkhous. (These concentrations are only approximate and are presented only to give general idea of results that have been obtained.) From Grossman.[6]

of the blood to heparin is said to be increased when a dilution of heparin, in the lower ranges, changes the whole blood clotting time more than it would the blood of a normal individual.

Clot lysis was determined by gross observation only. If, after 24 hr., cells were present in the bottom of the tubes used for the whole blood clotting time, lysis was said to be present. If the clot had remained whole and no cells could be seen in the bottom of the tube at that time, clot lysis was reported as absent.

All blood was obtained by arterial or venous femoral puncture, using a 20 gauge needle and an oiled 20 cc. syringe.

RESULTS

The results obtained on the 21 infants studied serially on the first, third and fifth days of life are presented in table 1. None of these infants had any clinical evidence of bleeding. None had received vitamin K, and none of the mothers was given vitamin K supplementation. It is apparent from the data that there is a great variability in the coagulation of the blood in the individual infants.

The variability, shown by the prothrombin levels, is illustrated by several cases. Cases 7 and 8 have values similar to those demonstrated by curves 1 and 2 (chart 1) which show a relatively normal prothrombin concentration on the first day of life, falling to the lowest levels on the third day of life and returning to normal or near normal levels on the fifth day. Cases 5 and 6 have values similar to curves 3 and 4 (chart 1) which show low levels of prothrombin on the first day of life with the level increasing progressively through the fifth day of life. Case 2 is similar in form to curve 5 (chart 1) which shows a low

prothrombin level on the first day and rises to normal by the third day and remains there. In addition, the authors have demonstrated in Case 14 that the level can be 100% of normal at birth, drop to only 92% on the third day, and return to 100% of normal on the fifth day. Also, Cases 1 and 12 demonstrate that the level may be normal at birth and fall progressively through the fifth day of life. Interestingly enough, if the figures for

TABLE 1

NORMAL BABIES

Case No.	Whole Blood Clotting Time in Minutes	Protamine Titration in μg. of Protamine	Prothrombin Time in % of normal	Platelets in 1000's/cmm.	Presence of Clot Lysis	Whole Blood Clotting Time in Minutes	Protamine Titration in μg. of Protamine	Prothrombin Time in % of normal	Platelets in 1000's/cmm.	Presence of Clot Lysis	Whole Blood Clotting Time in Minutes	Protamine Titration in μg. of Protamine	Prothrombin Time in % of normal	Platelets in 1000's/cmm.	Presence of Clot Lysis
	<6 hr.					3rd Day					5th Day				
1	9′	120	100	349	0	12′	120	77	375	0	24′38″	120	69	304	0
2	8′	140	58	204	++	10′	120	83	218	+	6′	120	83	—	0
3	12′	140	37	203	++	42′	160	26	210	0	<6′	QNS	54	—	0
4	8′	140	100	150	++	31.5′	140	69	240	+	5′40″	120	100	245	0
5	23′50″	120	40	218	0	25′30″	120	74	259	0	30′	120	82	234	0
6	28′	120	49	324	++	39′	140	65	—	+	32′	120	79	280	0
7	18′	120	100	353	++	30′	140	56	390	0	30′	120	91	320	0
8	31′	120	96	350	++	14′	140	65	370	0	14′45″	120	100	331	0
9	13′30″	140	71	250	+	13′	120	57	301	0	<6′	120	77	—	0
10	9′	120	55	220	+++	26′	120	53	311	+++	16′	120	73	—	0
11	32′	120	57	285	0	36′	120	50	—	0	10′	120	100	240	0
12	17′	120	92	265	0	10′	120	78	—	0	23′50″	120	77	249	+
13	17′	120	92	—	++	20′	120	77	300	0	19′	120	80	250	+
14	10′	120	100	—	++	10′	120	92	265	0	12′	120	100	276	0
15	38′27″	120	83	—	+	25′	120	55	250	0	<6′	120	86	260	0
16	23′	120	70	261	0	45′	120	51	250	0	27′	120	89	237	0
17	7′	120	88	248	0	19′	120	67	214	0	<6′	120	73	262	0
18	17′	140	75	222	0	31′	140	68	296	0	22′	120	100	204	0
19	14′	140	50	202	+	33′	140	30	202	0	38′	120	93	246	0
20	25′	120	80	214	0	12′	120	91	210	0	11′	120	96	240	0
21	9′	120	98	194	++	18′	120	88	230	0	7′	120	94	250	0

each of the three days had merely been averaged a curve would have been obtained similar in form to the Quick curve (Curve 1 in chart 1).

This variability is again illustrated by the whole blood clotting time which ranged between 7 and 38 minutes in the group measured within the first six hours of life. On the third day of life the range was from 10 to 60 minutes, and on the fifth day, from 6 to 38 minutes. As with the prothrombin levels it can be seen that the serial coagulation times in any one individual infant follow no particular pattern. However, if the coagulation times for each group are averaged, the highest value (25 minutes) will be found on the third day of life. The average time for the first six hours of life was 14 minutes and on the fifth day of life, 16 minutes.

The protamine titration, as compared with normal adult values, was found to be increased in 6 of 21 babies in the first six hours of life and 7 of 21 babies on the third day of life. No infant showed an increase on the fifth day of life.

All platelet values were considered to be within normal limits for the method used.

In the 21 infants studied serially, 13 showed gross evidence of clot lysis within the first

TABLE 2

Day	Case No.	Whole Blood Clotting Time in Minutes	Protamine Titration in μg. of Protamine	Prothrombin Time in % of Normal	Platelets in 1000's/cmm.	Presence of Clot Lysis	Heparin Sensitivity Expressed as clotting time in minutes									
							Dilutions in μg. of Heparin									
							C	0.1	0.3	0.5	0.7	0.9	1	2	3	4
I	1	6	120	92	209	0	4	11	24	32	32	37	48	82	119	
	2	7	120	100	235	0	6	24	53	54	56	58	58	66	91	117
	3	12	120	68	270	0	9	15	21	25	35	35	52	66	77	102
	4	16	120	100	276	0	4	4	14	21	26	31	35	44	75	106
	5	13	120	91	—	+	10	10	29	29	40	45	57	69	103	106
II	6	21	120	58	121	0	10	10	23	37	41	45	45	63	77	105
	7	30	120	52	137	0	8	16	20	27	35	35	53	67	86	101
	8	10	120	62	221	0	5	5	18	18	23	28	45	45	85	102
	9	27	120	82	201	++	11	18	40	40	55	55	62	99	107	110
	10	35	120	57	238	0	14	30	30	37	37	45	45	77	97	127
III	11	11	120	97	—	0	13	13	22	34	40	46	52	76	94	137
	12	21	120	75	—	0	7	13	24	31	31	41	41	58	73	98
	13	39	120	84	360	0	14	21	27	42	42	49	57	79	97	108
	14	60	120	67	187	0	26	37	50	57	62	67	71	92	111	137
	15	11	120	100	165	0	7	7	16	16	22	27	40	47	70	82
IV	16	19	120	100	221	0	6	10	24	33	33	33	37	56	82	102
	17	11	120	100	290	0	7	11	29	29	38	38	38	54	71	79
	18	10	120	82	320	0	4	6	12	22	29	29	35	69	90	90
	19	11	140	71	128	0	4	6	6	23	23	32	32	57	112	225
	20	22	120	85	216	0	12	19	21	27	27	35	42	74	82	108
V	21	10	120	92	312	0	2	3	3	3	12	18	33	48	69	75
	22	12	120	83	182	0	3	8	14	23	29	29	29	57	69	131
	23	9	120	100	325	0	3	3	3	3	11	17	17	49	66	78
	24	10	120	82	253	0	12	14	24	33	33	40	45	63	87	136
	25	19	120	100	219	0	14	18	24	41	41	77	84	90	110	140
VI	26	10	120	100	—	0	4	4	4	6	12	12	20	28	57	97
	27	25	120	86	—	0	8	19	25	65	65	73	80	108	121	160
	28	12	120	97	287	0	5	5	9	9	20	26	32	41	54	75
	29	34	140	100	232	0	11	18	26	37	37	49	49	64	81	104
	30	17	120	86	240	0	5	10	17	24	28	28	28	50	70	89
VII	31	25	120	100	279	0	8	16	22	26	32	32	37	54	63	93
	32	10	120	120	237	0	3	3	7	7	16	27	34	47	77	83
	33	9	120	97	102	0	4	7	10	18	18	27	32	38	48	65
	34	12	120	86	198	0	2	—	6	8	12	19	19	36	47	53
	35	10	120	80	328	+	11	17	17	27	27	34	42	65	76	76

six hours of life; 4 on the third day of life; and 2 on the fifth day of life. In no instance was the lysis of the clot complete.

The results of the heparin sensitivity tests are shown in table 2. In order to visualize the results more easily, representative days are shown graphically. The values obtained for the first day of life are shown in chart 2, while charts 3 and 4 show the values for days three and five, respectively. In charts 2, 3 and 4, it can be seen that there is considerable variation among individual infants for any given day. If the results of each of the first seven days of life are merely averaged (chart 5), it would appear that the greatest sensitivity to heparin was on the third day. However, the range of all the average curves is less than the range in the individual curves for any one day.

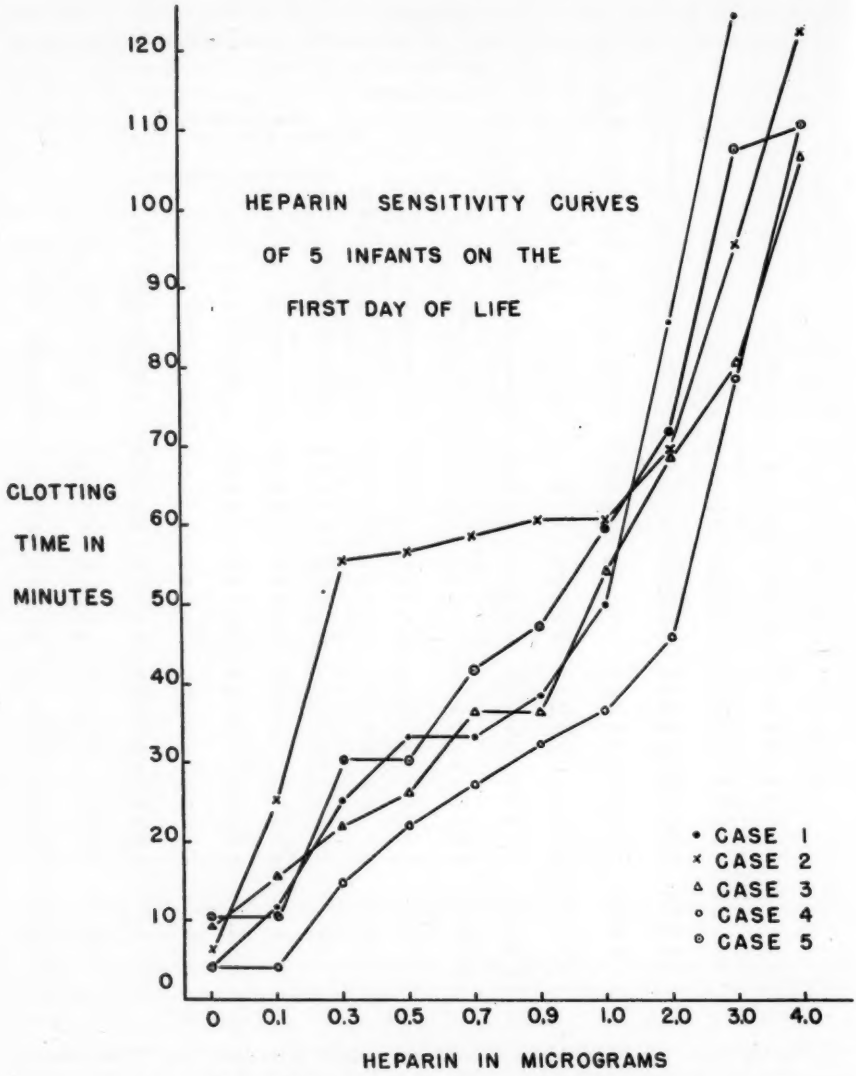


CHART 2. Heparin sensitivity curves on 5 infants on first day of life. (Case numbers correspond to those found in table 2.)

DISCUSSION

The problems encountered in obtaining whole blood from the newborn infant are greater than those encountered in drawing blood from older children or adults. These difficulties are (1) obtaining a clean puncture void of tissue juice, (2) maintaining a free flow of blood from these small vessels, (3) avoiding the entrance of air bubbles into the

syringe while drawing the blood and (4) obtaining the necessary amount of blood within a reasonable length of time (one minute). The whole blood clotting time is the test which is most easily distorted by any aberration in technic. It would seem that the coagulation times obtained in the lower ranges can be explained on this basis.

From the results obtained by averaging the data, the authors have, in general, agreed

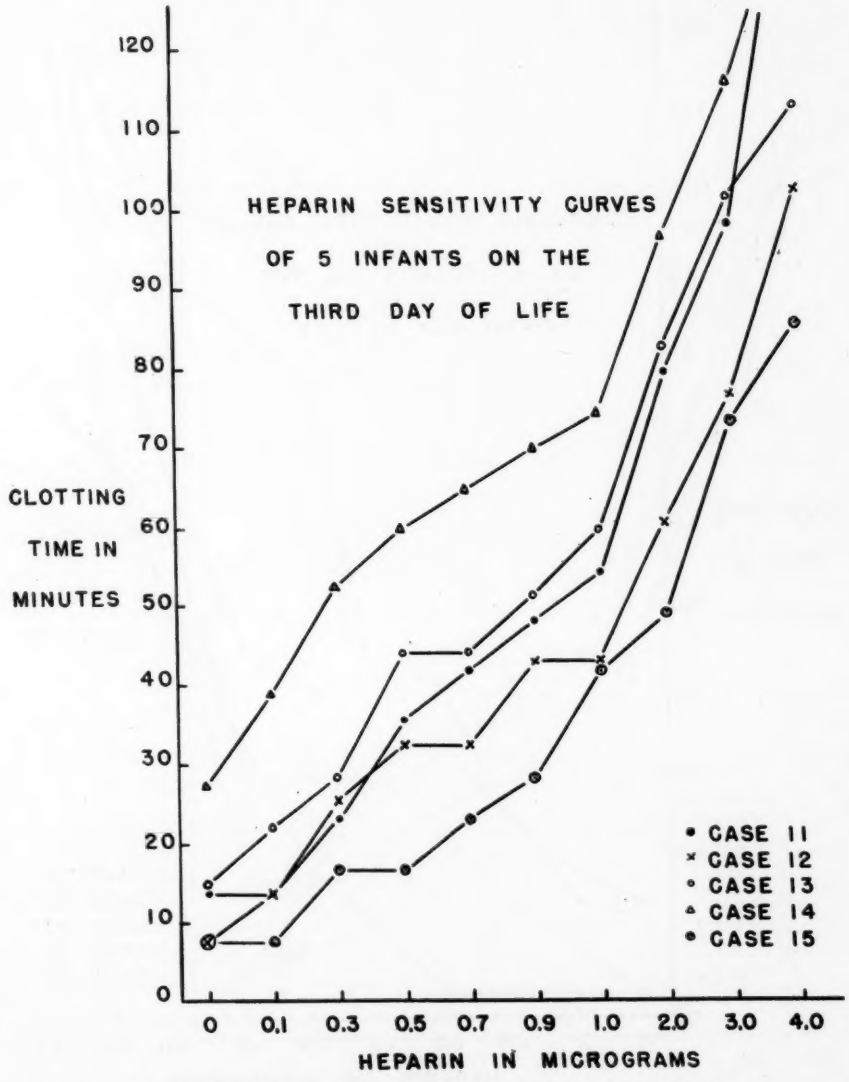


CHART 3. Heparin sensitivity curves of 5 infants on third day of life. (Case numbers correspond to those found in table 2.)

with the observations of other investigators. However, in examining the data on individual infants studied serially, it was found that most of the babies do not conform to the pattern obtained by averaging the figures for the group. Therefore, the pattern of a single infant cannot be considered as abnormal simply because it varies from the average group figures.

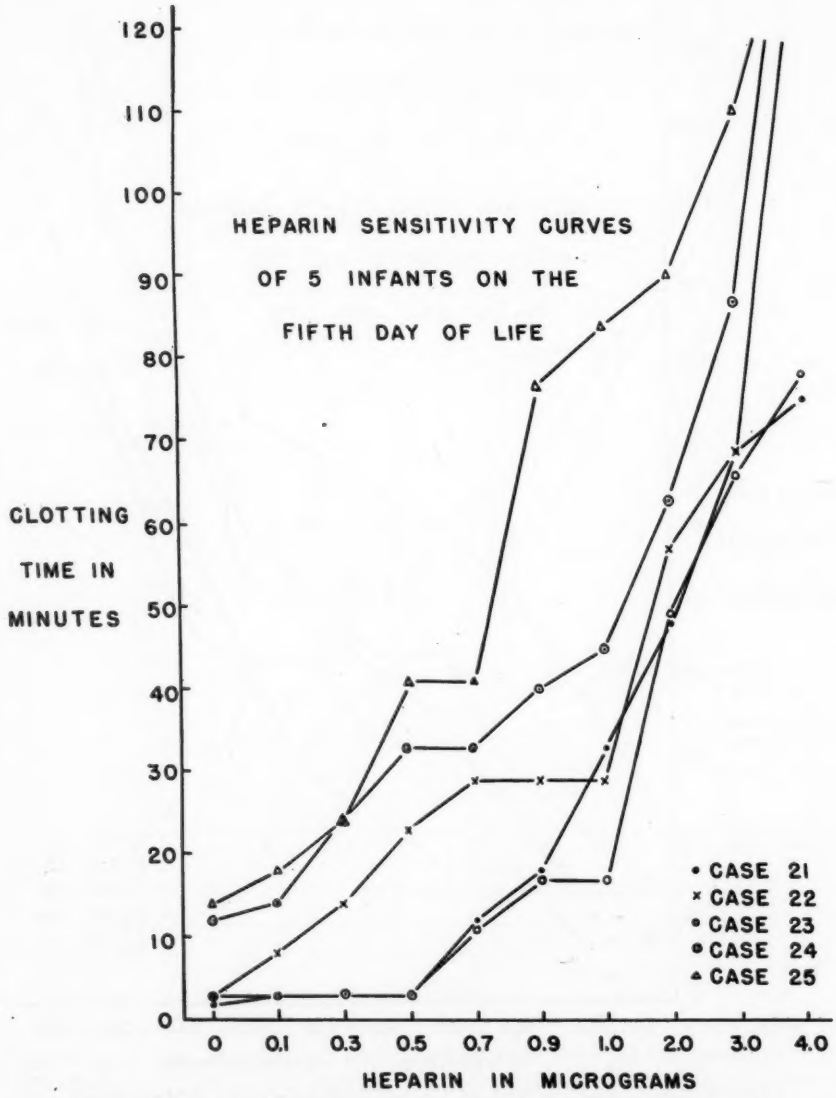


CHART 4. Heparin sensitivity curves of 5 infants on fifth day of life. (Case numbers correspond to those found in table 2.)

By using multiple technics the authors have attempted to evaluate a number of factors in the pattern of coagulation of the newborn infant. It can be seen from the data that the results of one or more of the technics employed in a single infant may be considered abnormal as compared with accepted standards, and yet that infant may have no evidence of hemorrhage. This is demonstrated by the following cases which had an abnormality of only one of the test methods used: (1) Case 13 (table 2) which had a whole blood

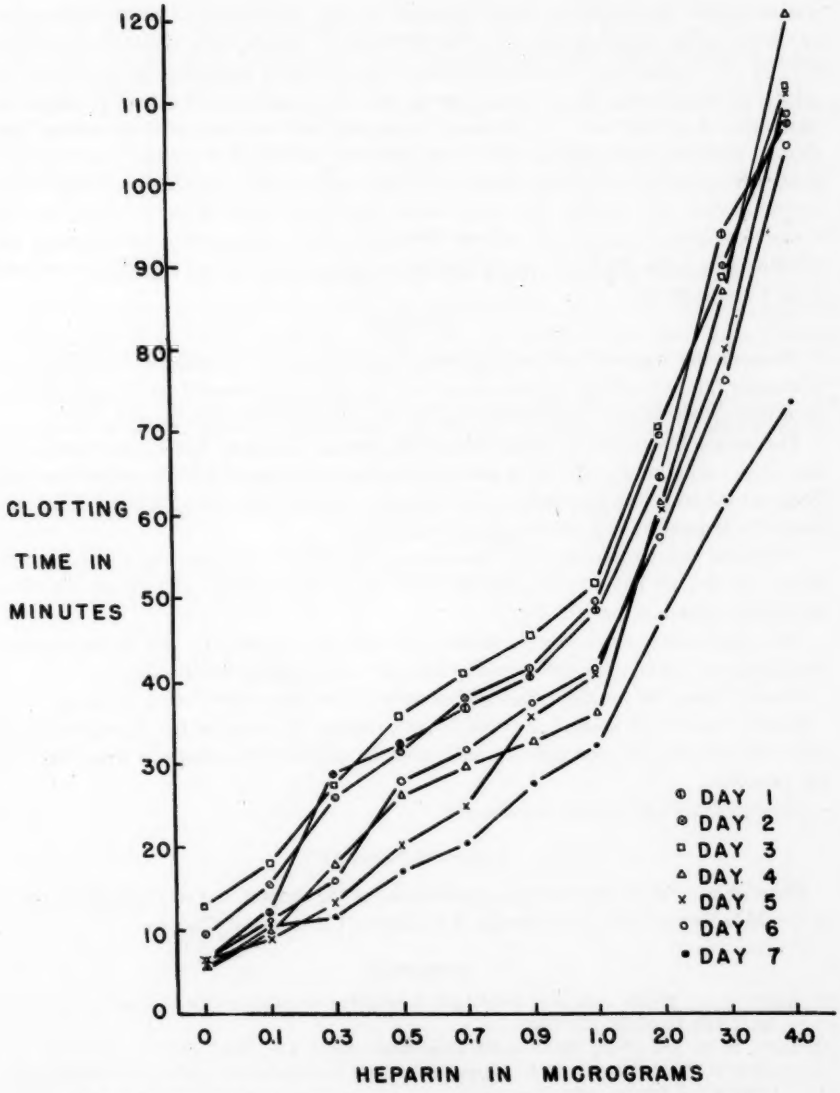


CHART 5. Average heparin sensitivity curves of 5 infants on each of 1st 7 days of life.

clotting time of 39 minutes on the third day of life, (2) Case 4 (table 1) which had a protamine titration of 140 μg. of protamine, (3) Case 5 (table 1) which had a prothrombin concentration of 40% on the first day of life and (4) Case 27 (table 2) with an increased heparin sensitivity on the sixth day of life. Other infants had abnormalities of 2 or 3 factors without evidence of bleeding. These included (1) Case 3 (table 1) which had a 42 minute whole blood clotting time, a 160 protamine titration, and a 26% prothrombin concentration on the third day, (2) Case 14 (table 2) which had a 60 minute whole blood clotting time, increased heparin sensitivity and 67% prothrombin concentration on the third day, (3) Case 29 (table 2) which had a whole blood clotting time of 34 minutes and a protamine titration of 140 μg. of protamine and (4) Case 16 (table 1) which had a whole blood clotting time of 45 minutes and a 51% prothrombin concentration on the third day. It should be pointed out that most of those infants who showed multiple abnormalities were in the third day of life. It is possible that if all the tests gave abnormal values simultaneously in the same infant a bleeding tendency might be manifested. It is realized that other factors than those tested might be concerned and a more complete study should include fibrinogen levels, prothrombin consumption and antithrombin levels. However, one is limited in the amount of blood that can be removed from a single infant.

Summary

Data on the whole blood clotting time, platelet count, prothrombin concentration, protamine titration and gross observation for clot lysis are presented on 21 normal newborn infants within six hours of birth, and on the third and fifth days of life.

The whole blood clotting time within the first six hours of life ranged from 7 to 38 minutes with an average of 14 minutes. On the third day of life the range was from 10 to 60 minutes with an average of 25 minutes. On the fifth day of life the range was from 6 to 38 minutes with an average of 16 minutes.

Protamine titration was increased as compared to normal adult values in 6 of 26 infants within the first six hours of life. On the third day 7 of 26 showed an increase. All titrations were normal on the fifth day.

The prothrombin concentration showed all variations of patterns, the average pattern being high on the first day, lower on the third day, and high on the fifth day.

Platelet values for the three days studied were all within normal limits, for adults.

Further data on 35 normal newborn infants, studied in groups of five through the first seven days of life using the above technics with the addition of the heparin sensitivity test, are presented.

The significance of the data is discussed.

Acknowledgment

The authors wish to express their appeciation for the support and encouragement given by Dr. Mila Pierce, Associate Professor of Pediatrics, University of Chicago.

References

1. Rodda, F. C., Studies with new method for determining coagulation time of blood in newborn, Am. J. Dis. Child. **19**:269, 1920.
2. Lucas, W. P., and others, Blood studies in newborn, Am. J. Dis. Child. **22**:525, 1921.
3. Sanford, H. N., and Leslie, E. I., Substances involved in coagulation of blood of newborn, Am. J. Dis. Child. **51**:590, 1936.

4. Sanford, H. N., and Shmigelsky, I., Quantitative and qualitative platelet values of normal newborn infants, Am. J. Dis. Child. **63**:729, 1942.
5. Gray, W. E., and Kelley, O. R., Prothrombin studies, especially in newborn, Am. J. Clin. Path. **10**:154, 1940.
6. Grossman, A. M., Coagulation defects in infancy and childhood, J. Pediat. **19**:205, 1941.
7. Allen, J. G., Moulder, P. V., and Enerson, D. M., Evaluation of in-vitro clotting time of whole blood, Argonne National Laboratory, 4474, Progress report: Abnormal bleeding, March 1950.
8. Baar, H., and Stransky, E., Die klinische Hematologie des Kindesalters, Leipzig and Vienna, Franz Deuticke, 1928, p. 314.
9. Quick, A., On quantitative estimation of prothrombin, Am. J. Clin. Path. **10**:154, 1935.
10. Allen, J. G., and others, Protamine titration as indication of clotting defect in certain hemorrhagic states, J. Lab. & Clin. Med. **34**:473, 1949.
11. Allen, J. G., and others, Abnormal bleeding: Response to treatment with toluidine blue and protamine sulfate, J.A.M.A. **139**:1251, 1941.
12. Allen, J. G., and others, Abnormal bleeding, Surg., Gynec. & Obst. **89**:692, 1949.
13. Waugh, T. R., and Ruddick, D. W., Test for increased coagulability of blood, Canad. M.A.J. **50**:542, 1944.

SPANISH ABSTRACT

Estudios de la Coagulación en Niños Recién Nacidos Normales

Los autores presentan data sobre el tiempo de coagulación de la sangre total, conteó de plaquetas, concentración de protombina, titraciones de protamina, y en la observación visual de la retracción del coagulo de 21 niños durante las primeras seís horas de nacido y durante el tercer y quinto día de nacido.

También se presenta data adicional obtenida en 35 niños recién nacidos normales, los cuales fueron estudiados en grupos de cinco durante los siete primeros días de nacidos, usando los mismos métodos arriba descritos y además pruebas de sensitividad a la heparina.

Se discute la significancia de la data obtenida en este estudio.

920 East 59th Street

BRAIN ABSCESS ASSOCIATED WITH CONGENITAL HEART DISEASE

By REGINA GLUCK, M.D., JOHN W. HALL, M.D., AND LOUIS D. STEVENSON, M.D.
New York City

CLINICIANS have long recognized brain abscess to be a complication of congenital heart disease. Rarely, however, has the diagnosis been made in time for successful therapy to be instituted. The purpose of this paper is to review the salient clinical features of cases of cerebral abscess with congenital heart disease, in the hope that recognition of these will make possible an early diagnosis. The various physiologic and pathologic theories offered in explanation of the correlation between the two conditions will be discussed.

The earliest reported case of brain abscess associated with congenital heart disease is found in the book by Farre[1] published in 1814; however, Ballet[2] in 1895 was the first to emphasize the correlation between the two conditions. He collected four cases (two of which seem to be identical) previously published and added one of his own. He insisted there must be an etiologic connection between the abscess and the congenital anomaly of the heart, and carefully noted that there were no other factors to explain the abscess. Fourteen cases were collected from the literature by Abbott, Lewis and Beattie[3] and two of their own cases added. Wechsler and Kaplan[4] published the case histories of two patients; the diagnosis of brain abscess was correctly made, but both patients died after operation. An excellent summary of the literature was made by Hanna[5] who published the clinical and autopsy findings in 23 cases including six of his own. Robbins[6] reported three cases, and attempted without success to produce experimentally cerebral abscess in rabbits. The first patient on whom the diagnosis of brain abscess was made and surgical treatment instituted successfully was reported by Smolik, Blattner and Heys[7] in 1946.* Gates, Rogers and Edward[8] published five cases, two of whom were operated on unsuccessfully. Recently two cases have been reported by Sweeney and Patton[9] and one case by Cohen, Bergman and Malis[10] that were treated successfully with surgery and antibiotics.

The incidence of the association of congenital heart disease and cerebral abscess has ranged from 0.7 to 7.0% in various reports. In the classic series of 1000 cases of congenital heart disease reported by Abbott,[11] seven (0.7%) had cerebral abscess.† However, the total number of cases in which the brain was examined is unknown. Hanna[5] reported six cases (3.7%) of cerebral abscess in 160 cases of congenital heart disease and Robbins[6] found three cases (5.6%) with abscess in a series of 53 cases of congenital heart disease.

From the Departments of Pediatrics, Pathology and Neuropathology of New York University College of Medicine and Bellevue Hospital, New York City.

(Received for publication July 6, 1950.)

* A personal communication from the authors states that the patient was well 4 years later.

† Three cases of pulmonary stenosis with patent foramen ovale and defect of interventricular septum, one case of pulmonary stenosis with closed foramen ovale and with defect of interventricular septum, one case of aorta arising from both ventricles, one case of communication between aorta and pulmonary artery, one of pulmonary atresia with defect of ventricular septum and closed foramen ovale.

In a study of 13,883 autopsies, Maronde[12] found 15 cases (7.1%) of brain abscess in 209 cases of congenital heart disease. In the present authors' series of 59 cases of congenital heart disease, 39 with complete postmortem examinations, there were three cases (7.0%) of brain abscess. Evans[13] reported 194 cases of cerebral abscess found at autopsy at the London Hospital between 1908-1925. In 17 of these cases the sources of the abscess could not be shown conclusively. He carefully noted the presence of a patent foramen ovale in 15 of these cases (one in addition had a ventricular septal defect). Without any data on the cardiac findings in the other 179 cases, it is difficult to evaluate incidence from Evans' series of cases.

In reviewing the literature, the authors have selected cases with necropsy findings; if these were not available, only those cases are included in which there was indisputable clinical and laboratory evidence of both congenital heart disease and brain abscess (such as cranial air studies outlining the abscess followed by aspiration of pus from this area). Forty-one cases could thus be selected from this review and in addition three of the authors' are presented in detail (table 1).

In the total of 44 patients, 22 were male and 22 were female. Twenty patients were 10 years of age or younger, 15 were in the 10 to 20 year age group, 4 were between 20 to 30 years old, 4 were in the 30 to 40 year age group, and 1 patient was in the 50 to 60 year age group. The youngest patient was 3 years old, the oldest 57. It is of particular interest that 23 cases (52%) were within the pediatric age group—under 13 years of age. Twenty-one of the brain abscesses were in the right hemisphere, 19 were in the left hemisphere, 1 was interventricular, 1 was in the cerebellum, 1 was bilateral and no localization was given in 1 case. In 90% of the cases, the abscess were single, the remainder were multiple. These statistics are of especial interest because it is the solitary brain abscess that is amenable to surgery.

Ten of the reviewed cases of cerebral abscess associated with congenital heart disease have had cranial operations (table 2). In four patients the operations were successful, although two patients had meningitis prior to surgery. The remaining six patients died postoperatively; in one case there are no clinical data available. There was no evidence of meningitis prior to the initial operation in the other five patients.

In a review of the literature a definite history of recent infection, such as gingivitis and bronchitis, or of surgery, such as tonsillectomy, adenoidectomy and appendectomy, was found in only eight cases. A vague history of an upper respiratory infection was elicited in five; the other 30 patients were previously in good health except for the cardiac condition. In the reported cases the chief and earliest symptom was headache, most frequently frontal, occasionally localized over the orbit or over the ear. Lethargy and vomiting were symptoms in many of the cases. Fever was present at the onset in only about half the patients. Later symptoms were convulsions and weakness of the extremities or of the face. Meningeal signs, although absent at the onset, were present before death in about half of the cases. On admission to the hospital, frequently the white blood cell count was normal, and the spinal fluid clear. One must realize that the classic picture of brain abscess with fever, localizing central nervous system signs, elevated white blood cell count, and pleocytosis of the spinal fluid may be absent. It is precisely in the absence of these positive findings that the best results may be obtained from surgical intervention. Once the abscess has ruptured into the ventricular system or subarachnoid space producing meningeal signs, treatment with antibiotics alone did not prevent death. The occurrence

TABLE 1

Author	Age (yr.) and Sex	Cyanosis	Cardiac Lesion	Cerebral Lesion
Farre[1] 1814	9½ M	Yes	Tetralogy of Fallot	Abscess R hemisphere
Berthody[19] 1845	21 F	Yes, after exertion	Tetralogy of Fallot	Abscess L posterior lobe; numerous red points in brain
Ballet[2] 1880	15 M	No	Cor triloculare biatrium	Single abscess R frontal and parietal lobes
(From Lallemand)	57 F	Yes	Tricuspid stenosis, I-A defect; subpulmonic stenosis	Abscess ant. part R hemisphere; surrounding brain very red
Stone[20] 1881	19 F	Yes	Tetralogy of Fallot	Abscess R lower occipital lobe
Northrup[21] 1894	4½ M	Yes	Tetralogy of Fallot	Location not given
Jacobi[22] 1895	26 M	Yes	I-V defect; thick tricuspid; small aorta	Abscess L temporo-sphenoidal region
Acker[23] 1895	6 F	Yes	Transposition; closed patent ductus; I-V defect; patent foramen ovale	Abscess R tempero-sphenoidal region
Deneke[24] 1906	18 M	Yes	Cor triloculare biatrium; transposition; small patent ductus; closed foramen ovale	Abscess R hemisphere
Heigel[25] 1913	10 F	No	R auricle, R ventricle continuous; patent foramen ovale	Abscess L frontal lobe
Abbott, Lewis and Beattie[3] 1923	11 M	Yes	Tetralogy of Fallot	Abscess L frontal lobe
Raab[26] 1923	15 M	Yes	Pulmonary stenosis; I-V defect; patent foramen ovale	Abscess R hemisphere.
Bach[27] 1928	30 M	Yes	Tetralogy of Fallot	Abscess R posterior temporal region
Baumgartner and Abbott[28] 1929	20 M	Yes, of dependent parts	Tetralogy of Fallot; deformed tricuspid	Abscess R fronto-parietal region
Rabinowitz, Weinstein and Marcus[29] 1932	16½ F	Yes	Tetralogy of Fallot	Abscess in cerebellum
*Drey, Strauss and Gray[18] 1938	14 F	Yes	Cor triloculare biatrium; anomalous insertion intercostal veins into pulmonary veins	Interventricular abscess
Ingham[30] 1938	39 F	Yes	Patent foramen ovale; old thrombus in pulmonary artery with arteriosclerosis	Abscess L cerebrum
Hanna[5] 1941	18 F	No	Basal I-V defect; thickening edge of mitral valve	Abscess in L thalamus
	34 F	No	Basal I-V defect with valve	Abscess L frontal lobe
	10 F	Yes	Tetralogy of Fallot; I-A defect; tricuspid valve thickened	Area hemorrhagic softening (histologic picture early abscess); red infarct posterior to area of softening
	3 M	Yes	Tetralogy of Fallot	Abscess R temporal lobe

TABLE 1—(*continued*)

Author	Age (yr.) and Sex	Cyanosis	Cardiac Lesion	Cerebral Lesion
Ruhberg[31] 1942	6 F	Yes	Pulmonary stenosis; I-V septal defect	Multiple abscess R occipital lobe
Vann and Miller[32] 1944	8 M	Yes, after exertion	Cor triloculare biatrium; transposition; pulmonary stenosis	Abscess both frontal lobes
Robbins[6] 1945	10 F	Yes	Tetralogy of Fallot	Abscess L parieto-occipital region
	19 F	Yes	Tetralogy of Fallot; patent ductus; pulmonary valve occluded by membranous septum	Abscess R parieto-occipital region
	20 F	Yes	Tetralogy of Fallot; patent ductus	Abscess L sup. temporal convolution
Sidenberg, Kessler and Wolpaw[33] 1946	6 M	Yes	Tetralogy of Fallot; chronic vegetations in pulmonary channel	Abscess R parietal region; anterior half corpus callosum and vermis absent
Gates, Rogers and Edward[8] 1947 (Mayo Clinic)	6 M	Not mentioned	Cor triloculare biatrium	Abscess L tempero-occipital region
	5 M	Not mentioned	Tetralogy of Fallot	Abscess L fronto-parietal region
	26 F	Not mentioned	I-A defect	Abscess upper R occipito-parietal region; infarction cortex R occipital lobe
Sancetta and Zimmerman[34] 1950	35 F	Not mentioned	Basal I-V defect; patent ductus	Abscess R temporal lobe
Authors' cases	4½ M	Yes	Tetralogy of Fallot	Abscess L occipital lobe; encephalomalacia L occipital and L temporal lobe
	7 M	Yes	Transposition of great vessels; I-A defect; I-V defect; pulmonic and subpulmonic stenosis; tricuspid mitral valve; hypertrophy and dilation of heart; organized and recanalized thrombi in pulmonary vessels	Abscess L temporal lobe; encephalomalacia involving posterior frontal region and temporal lobe
	12 M	Yes	Tetralogy of Fallot	Abscess L occipital lobe

* Thrombus renal art. and multiple thrombi lungs and kidney.

of persistent headache or lethargy in a patient with congenital heart disease deserves prompt and thorough investigation. Even if the spinal fluid is clear, the diagnosis of brain abscess must not be dismissed, electroencephalogram and cranial air studies should be done in an effort to localize the lesion. Once the diagnosis of abscess is made, surgical exploration should not be postponed. The abscess is usually single and well-localized and as such may be amenable to immediate surgery with supportive chemo- and antibiotic therapy.

TABLE 2

Author	Age (yr.) and Sex	Cyanosis	Cardiac Lesion	Cerebral Lesion	Operation
Wechsler and Kaplan[4] 1940	14 M	Yes, since birth	No post mortem	Aerograms showed abscess R parietal lobe; pus aspirated; open operation	3 wk. after onset of symptoms. Died 50 days post-op.
	11½ F	Yes, since birth	No post mortem	Aerograms showed abscess R parietal lobe; pus aspirated; open operation	Died 43 days post-op.
Smolik, Blattner and Heys[7] 1946	9 F	No	Murmur heard since age of 2 mo.; presumed to be I-V defect	Aspiration and open operation in L frontal area	4 wk. after onset of symptoms. **Successful**—4 yr. later: well, good mentally
Hand[38] 1947	4½ M	Yes	I-V defect; pulm. stenosis; vegetation on aortic valve	Pus aspirated from L temporal area; post mortem: 3 abscesses—L temporal, L occipital, L parietal lobes	Died—several days post-op.
	8 F	Not mentioned	Transposition of heart; L vent. almost atrophic, R aur. and vent. hypertrophied	1st operation, recovery; 2 wk. post-op. recurrence; 2nd operation, no pus from original site; at post mortem 2nd abscess filled whole R temporal lobe	Died—several wk. post-op.
Gates, Rogers and Edwards[8] 1947	8 M	Yes	Tetralogy of Fallot	Abscess R frontal lobe	7 wk. after onset of symptoms; died
	39 F	Yes	I-A defect; organizing mural thrombus attached to wall of L pulm. art. partially occluding lumen	Decompression done. Abscess L tempero-parietal region thought to be some some weeks old	1 wk. after onset of symptoms; died
Sweeney and Patton[9] 1950	10 M	Yes	Clinical diag.: Eisenmenger complex	Pus obtained through burr hole from L post-parietal region	7 wk. after onset of symptoms; **successful**—3 mo. later: well except for slight hemiparesis
	8 M	Yes	Blalock operation done in 1946	Abscess R occipito-parietal region	2 wk. after onset of symptoms; **successful**—12 days later: discharged well
Cohen[10]	22 F	Yes	Tetralogy of Fallot; patent ductus	Abscess R temporal lobe	**Successful**—1 yr. later: well

Case Reports

Case 1: F. R., a 4½ yr. old boy was first seen at age 3½ yr. for cardiac diagnosis. He was cyanotic at birth, and clubbing of fingers was noted in infancy; walking was delayed until age 2 yr. He was moderately underweight, with marked cyanosis of lips and nails; clubbing of fingers and toes was marked, and dyspnea was present on moderate exertion. The sternum bulged; heart was enlarged to L. There was a loud harsh systolic murmur maximal in 3rd ICS at L sternal border and widely transmitted. Fluoroscopy disclosed a typical *coeur-en-sabot* configuration; the ECG demonstrated a R axis deviation. Hgb was 18.5 gm./100 cc., RBC count 10.2 million/cmm. WBC count 9.4 thousand/cmm. Diagnosis of tetralogy of Fallot was made.

Nine months later he returned to the hospital with a temperature of 38.3 to 38.8°C.; he had been vomiting during the past 9 days. He complained of weakness and general fatigue, but did not appear ill. Physical examination was the same as on previous admission, with additional finding of a mild

bilateral catarrhal otitis media. Otitis media was treated with sulfapyrazine for 3 days, when the drug was discontinued because of crystalluria. During his first week in the hospital, temperature ranged from 37.2 to 38.3°C. (with several intervening days of normal temperature). He complained of "feeling sick" and of severe frontal headache, and also vomited several times. Otitis media improved, but cloudiness of L antrum was noted on RG. On 9th hospital day temperature rose to 38.6°, and WBC count from the admission count of 10.9 thousand/cmm. (79% neutrophiles) to 16.3 thousand/cmm. (84% neutrophiles); sulfadiazine therapy was started. Subacute bacterial endocarditis was suspected, but no petechiae were seen and blood culture was sterile. On 12th hospital day, because of continued fever, headache and vomiting, a spinal tap was done, although no meningeal signs were present. Fluid was ground glass in appearance, and under markedly increased pressure; there were 1120 WBC/cmm.; neutrophiles 30%, lymphocytes 70%; protein 41.6 mg./100 cc., sugar 14.7 mg./100 cc. Cl 121.9 mEq./l. and culture sterile. Temperature rose to 40.5°C. and WBC count to 21 thousand/cmm. (82% neutrophiles). Penicillin was given in addition to sulfadiazine. Spinal tap repeated on following day showed an elevated pressure with an increase of cells to 3880 (61% neutrophiles, 39% lymphocytes). Organisms seen on smear were suggestive of H. influenzae, and although they could not be typed, were more sharply demarcated with H. influenzae B antiserum; therapy with anti-influenzae serum was given intravenously. Patient was sleeping most of the day, but was alert when awake; marked ptosis of L eyelid was noted at this time. On 14th hospital day, he became comatose, and 4 hr. later died.

Clinical diagnosis was tetralogy of Fallot and meningitis secondary to sinusitis. On admission to hospital, the infection of the upper respiratory tract was considered sufficient explanation for symptoms. Brain abscess was not considered because the meningitis was thought to be secondary to sinusitis.

Positive findings at necropsy were tetralogy of Fallot and an abscess in L occipital lobe with a purulent meningitis, most extensive over occipital lobe. Abscess was surrounded by an area of encephalomalacia that extended from temporal to the occipital lobe. Histologic examination revealed abscess to be surrounded by a capsule composed of granulation tissue.

Case 2: C. deR., a 7 yr. old boy, was first seen at age 6 yr. for cardiac diagnosis. He had been cyanotic since birth. Mental development was normal; he did not walk until 3 to 4 yr. of age, but then became quite active. He was well developed and well nourished with striking cyanosis of lips, skin and nails and moderate clubbing of digits. A systolic thrill was present in 3rd L ICS, and a loud, long, harsh systolic murmur was heard maximal at the 2nd and 3rd ICS to L of sternal border and transmitted to entire precordium. P_2 was loud and snapping. Blood pressure was 90/75 mm.Hg. Roentgenographic examination in frontal view showed slight cardiac enlargement with apex rounded although not raised, and narrowing of shadow of great vessels; lungs were moderately congested. There was a questionable enlargement of R ventricle in LAO view and pulmonary window showed only slight increased clarity. In RAO view good pulsation but no enlargement was seen in region of pulmonary artery segment. There was marked R axis deviation with high notched P waves. Hgb. 16 gm./100 cc., RBC count 8.9 million/cmm., WBC count 10.3 thousand/cmm. with normal differential count. Tuberculin test was negative. Clinical impression was probable transposition of great vessels with associated septal defects of considerable size to account for the fairly good functional capacity. Cardiac catheterization was deferred because of a respiratory infection. Six months later and just 2 wk. before the onset of his terminal illness, he was examined at a Health Station for admission to school, and was found well aside from his cardiac condition.

Eight days before final admission he suddenly complained of frontal headache. His appetite was poor; he was lethargic and had a temperature of 39.4°C. He was given sulfonamide therapy for 2 days without beneficial effect. During the next 6 days fever, headache, lethargy and anorexia persisted. On admission to hospital on 8th day of illness, patient constantly complained of pain in frontal region, pain in neck, and of photophobia. He was drowsy and irritable though cooperative. Temperature 37.7°C., PR 80/min., R. 24, BP 86/70 mm.Hg. Cardiac findings were unchanged; tonsillitis and cervical adenitis were present. He had positive Kernig and Brudzinski signs, equal bilateral depression of deep tendon reflexes and a bilateral Babinski sign. Spinal fluid was opalescent, under normal pressure, containing 597 WBC/cmm. (95% mononuclears); Pandy ++, protein 54.4 mg./100 cc., sugar 62 mg./100 cc., Cl 119 mEq./l. No organisms were seen on smear, and cultures were sterile. Nose and throat cultures were overgrown with Staph. aureus hemolyticus. Skull RGs were negative. At this time Hgb. was 20.5 gm./100 cc., RBC count 7.2 million/cmm., WBC count

9.3 thousand/cmm. (neutrophiles 76%). Therapy was withheld pending report of spinal fluid culture. Although no causative organism had been isolated penicillin was given on 10th hospital day. Twelve hours later, he became comatose, temperature rose to 40.0°C., respirations became gasping, and 10 hr. later he died.

Clinical diagnosis was transposition of great vessels and meningitis, probably of viral etiology. Cerebral abscess was considered unlikely in this case because of short history, normal temperature after subsidence of tonsillitis, normal WBC count and differential, absence of localizing signs in central nervous system, and marked preponderance of mononuclear cells in the spinal fluid.

Pertinent autopsy findings were complete transposition of great vessels, interatrial and interventricular septal defects, stenosis of pulmonary valve, subpulmonic stenosis, a tricuspid mitral valve, hypertrophy and dilation of heart. In addition, there were organized and canalized thrombi in pulmonary vessels. A large abscess was present involving L temporal lobe and extending from the posterior horn of L lateral ventricle, almost to the surface of brain. There was a purulent meningitis over the cortex in this region. Abscess was surrounded by a large area of encephalomalacia involving L posterior frontal region and temporal lobe. Histologic examination revealed the abscess to be surrounded by a fairly well-developed capsule of fibrous tissue.

Case 3: M. R., a 12 yr. old Puerto Rican boy, was first seen at the age of 11½ yr. for consideration of cardiac surgery. He was supposedly normal at birth; cyanosis was first noted at age of 1 yr. and progressively increased. He was unable to walk until he was 9 yr. old, and then only a few steps, because of dyspnea. At age of 11½ yr., he was admitted to another hospital because of fever of 38.8 to 39.4°C. Eight blood cultures were taken, but there was no growth aerobically or anaerobically. However, he was given penicillin 1.6 million units daily for 10 days without any effect on fever. Temperature gradually returned to normal during following months, and he was then transferred to this hospital for possible cardiac surgery. He was underdeveloped and unable to stand long because of dyspnea and giddiness; he assumed the "squatting position" even in a wheel-chair. Cyanosis was striking and the digits had a "drumstick" appearance. PMI was in 5th interspace within the midclavicular line. There was a moderately loud, rough systolic murmur at 3rd ICS at L sternal border fairly well localized. PR 100/min., BP 106/86 mm.Hg. ECG demonstrated a R axis deviation. Hgb. 20.5 gm./100 cc., RBC count 9.5 million/cmm., WBC count 6.6 thousand/cmm. (neutrophiles 69%). Fluoroscopy revealed a typical *coeur-en-sabot* configuration, clarity of pulmonary window and diminished vascularity of lungs.

Diagnosis was tetralogy of Fallot with marked pulmonary stenosis or possible pulmonary atresia. Cerebral abscess was suspected because of previous unexplained fever, and therefore a spinal tap and EEG were done. Spinal fluid findings were normal. Electroencephalogram was within normal limits except in posterior parietal region bilaterally. Findings suggested possible midline abnormality or an abnormality reflected from deeper regions. During 1st 10 days of hospital stay, the temperature occasionally rose as high as 38.3°C., but was normal for 4 days before discharge.

Five months later he was readmitted with a history of fever of 4 days' duration, nausea and vomiting for 2 days, some diarrhea, and pain in R eye. Hematemesis had occurred the night before admission. On examination he was semicomatose; cardiac findings were the same as previously described. T. 38.26°C., PR 80/min.; Kernig and Brudzinski signs were positive; knee jerks and ankle jerks were decreased bilaterally. There were searching movements of eyes and a questionable L lower facial weakness. Spinal fluid was cloudy, WBC count 7.0 thousand/cmm. (90% neutrophiles), protein 310 mg./100 cc., sugar 12 mg./100 cc. Hgb. 24 gm./100 cc., RBC count 10.3 million/cmm., WBC count 12.0 thousand/cmm. (neutrophiles 92%, lymphocytes 8%). Electroencephalographic findings were interpreted as similar to those seen in previous record but more abnormal; activity was most marked over occipital region and most severe over L occipital area; no definite localizations were seen but a gross intracranial lesion was indicated.

A diagnosis of brain abscess with rupture into subarachnoid space was made. Sulfadiazine and penicillin were given immediately, while arrangements were being made for surgical exploration. Temperature rose to 39.1°C., he sank deeper into coma, and died 17 hr. after admission.

It is interesting to conjecture whether the brain abscess was present on first admission, and signs and symptoms masked by the intensive chemotherapy given at the first hospital. In spite of normal spinal fluid findings cranial air studies should have been done on first admission when brain abscess was suspected.

Pertinent autopsy findings were tetralogy of Fallot and an abscess of L occipital lobe with purulent meningitis. Abscess measured 2 x 2½ cm. Histologic examination revealed an unencapsulated abscess.

An understanding of the pathogenesis of cerebral abscess depends largely upon recognition of the mode of transmission of the infecting organism. The general impression is that, except for direct implantation, the abscess is always secondary to some other focus of infection that reaches the brain from neighboring tissues by direct suppurative extension via blood vessels, Virchow-Robin spaces, or through preformed paths, such as nerve sheaths and foramina. The infection may also reach the brain by infected emboli or bacterial showers or by traversing the vertebral and epidural venous plexuses.[14]

Robbins[6] has assumed that cerebral abscess associated with septal defects of the heart are the result of paradoxic emboli, sterile or infected, producing an area of lowered

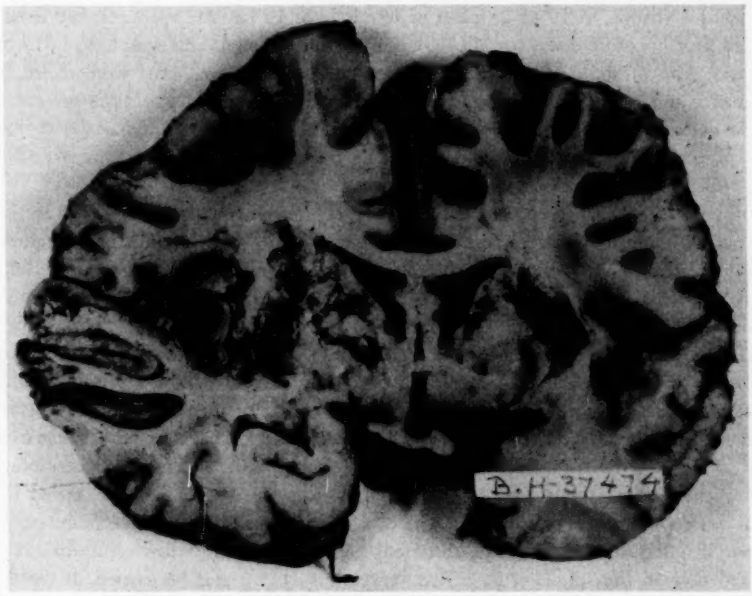


FIG. 1. Infarcts of brain with involvement in left hemisphere of caudate nucleus, part of putamen, insula, superior and midtemporal convolutions and lower parietal lobule. Right hemisphere reveals large infarct involving internal capsule and lenticular nucleus. Brain also revealed softening of both occipital lobes.

resistance followed in the former instance by bacteremia that infects the area of infarction. He makes the statement that "it is to be hoped that a study of a larger number of cases of congenital heart disease may reveal instances of encephalomalacia prior to their infection by organisms spread through the blood stream." Hanna[5] is also of the opinion that brain damage precedes the development of an abscess and states that two of his cases are probably examples of brain abscess that developed in areas of infarction. Two of the authors' cases (Cases 1 and 2) suggest a similar relationship. If these opinions and observations are correct, then one would expect to find examples of infarction associated with congenital heart disease but without evidence of abscess formation. The authors found this change in 5 of 39 brains examined. The area or areas of infarction were grossly visible in all five cases (Fig. 1).

A problem of importance is the mechanism by which these areas of infarction are produced. The theory mentioned, paradoxic emboli, although accounting for a rare case seems to be the least likely cause. This mechanism would postulate the presence of thrombi in the systemic veins to account for a source of paradoxic emboli. In congenital heart disease systemic venous thrombosis is rare.

Another source of emboli could be the lungs, with emboli entering the arterial circulation through the pulmonary vein, left auricle and ventricle. Spain[15] has reported systemic arterial embolization in cases of pulmonary tuberculosis with the source of the emboli being thrombus material in the pulmonary veins. The same source for emboli has been demonstrated in congenital heart disease by Rich.[16] He described pulmonary thrombi, both arterial and venous, in 19 of 21 cases of tetralogy of Fallot. An operation had been performed shortly before death for alleviation of the cardiac signs and symptoms in 17 of the 21 cases. The thrombi were in various stages of development, some were recent, some organizing and others organized and canalized. One of the problems in the present study was to determine the frequency of this vascular lesion in a consecutive series of various types of congenital heart diseases that had not been operated upon. Pulmonary thrombi were present in only 6 cases of the 59 examined.

Collis[17] has recently presented a theory for the development of brain abscess in the presence of thoracic disease and implies that this theory may explain the development of brain abscess in congenital heart disease, particularly in cases of tetralogy of Fallot.

His theory is based on the drainage of the bronchial and intercostal veins into the azygos veins; the spinal veins also drain into the azygos system. The spinal veins are valveless so that blood can flow in either direction. The thrombus starts close to an inflammatory lesion in the lung or pleural cavity and gradually extends from the capillaries to larger venules. "In order for it to spread to the vessels of the chest wall, it is necessary for the adhesions between the lung and the chest wall to have become vascularized." More commonly, the thrombi will affect the intercostal veins because the distribution of the bronchial veins is relatively limited. Emboli from this source will be carried to the azygos vessels, thence to the superior vena cava and then caught up in the pulmonary bed without ill effect. If, however, the thrombus becomes detached when conditions favor a reversed flow in the spinal veins, it may enter this system and be carried to the brain. These conditions will be present while coughing or straining at stool, or when the patient is lying supine. Having reached the brain, the embolus will become lodged at the venous end of the capillary and if infected will produce a brain abscess.

In the cases of congenital heart disease associated with pulmonary thrombi that the authors have examined, pleural adhesions, infection of the lung and infected thrombi have been absent, all of which are important conditions for the development of cerebral lesions according to Collis' theory.

In addition to embolization producing an area of infarction in the brain, the possibility also exists of thrombosis occurring in the cerebral vascular system in cases of congenital heart disease. None of the authors mentioned previously describes such an occurrence. Rich[16] states that a study of the other viscera in his cases of congenital heart disease with pulmonary thrombi failed to disclose any such tendency to thrombosis. He does not mention thrombosis of vessels in other situations in these cases. Drey, Strauss and Gray[18] reported a case of functional cor biatriatum triloculare that revealed in addition to a brain abscess, thrombosis of branches of the renal arteries with renal infarction and multiple capillary thrombi in the lungs and kidneys. In 3 of the present authors' 5 cases of

infarction, there were vascular thrombi that could account for the cerebral lesion. In one there was thrombosis of the right internal carotid artery, another had thrombosis of the internal carotid arteries and the third, thrombosis of cerebral arteries and the longitudinal sinus. The first of these three cases also had thrombosis of both iliac arteries and the left popliteal artery with beginning gangrene of the feet. The third case in addition to the cerebral thrombosis had thrombosis of renal arteries with infarction.

The exact mechanism of the production of thrombi in congenital heart disease is unknown although there are several possible explanations for their occurrence. In the type of congenital heart disease with venous-arterial shunts there is some degree of cyanosis and in an attempt to compensate for the anoxemia, a mild or marked polycythemia develops. The authors are not unaware of the fact that in conditions that reveal a secondary type of polycythemia, such as congenital heart disease, descriptions of thromboses other than pulmonary rarely have been published up to the present time. However, the only explanation that can be offered for the systemic thromboses in the present authors' cases is an increased viscosity of the blood secondary to polycythemia. According to Rich[16] another factor that favors pulmonary thrombosis in cases of congenital heart disease with pulmonary stenosis is the inadequate pulmonary blood flow. Circumstances that tend to slow the flow of blood in a vessel predisposes to thrombosis. In cases of pulmonary stenosis, the greatly reduced amount of blood delivered to the pulmonary circulation, with the consequent low pressure in the pulmonary artery, would be expected to reduce the rate of flow in the pulmonary vessels. It would seem that decreased flow of blood, due to increased viscosity secondary to polycythemia, and decreased pulmonary blood flow because of anatomic defects of the heart offer the most satisfactory explanation for the development of thrombi in congenital heart disease.

The authors' main interest has been directed to a study of the relationship of congenital heart disease and cerebral abscess. However, there are other conditions, such as mongolism, well known to be associated with congenital cardiac anomalies. For this reason, it seems to be of importance to list all the cerebral changes observed in the autopsy series. In the 39 brains examined there were, besides three with brain abscess and five with infarction, five others that presented a developmental defect and four with marked or massive cerebral and subarachnoid hemorrhage. In one of this latter group the diagnosis was hemorrhagic disease of the newborn. Five cases that were diagnosed clinically as mongolism also had changes of a nonspecific character in the cerebral convolutions of the brain. Thus significant cerebral changes were present in 22 of 39 cases of congenital heart disease.

Summary

A review of the literature reveals 41 adequately documented cases of cerebral abscess associated with congenital heart disease. Three cases of cerebral abscess occurring in 39 autopsied cases of congenital heart disease are reported in this paper.

The clinical signs and symptoms of cerebral abscess are presented with special emphasis on the need for early surgical intervention. The occurrence of persistent headache or lethargy in a patient with congenital heart disease should be thoroughly investigated. Spinal tap, EEG and cranial air studies should be done before the diagnosis of cerebral abscess is excluded.

Several authors believe that an area of infarction in the brain precedes the development of an abscess although this process alone has not been reported in congenital heart

disease. Five instances of cerebral infarction were observed in 39 autopsies on individuals with congenital heart disease.

A number of possible explanations have been offered for the development of infarction: paradoxic emboli, emboli from the lungs through the systemic arterial circulation by way of the pulmonary vein, left auricle and ventricle, emboli from the lungs through the spinal veins and finally, as a result of thrombosis of the cerebral arteries.

In addition to pulmonary and cerebral thrombosis, thrombi were found in the iliac, popliteal and renal arteries. The tendency to systemic and pulmonary thromboses in cases of congenital heart disease is best explained on the basis of decreased flow of blood due either to polycythemia or to decreased pulmonary blood flow.

Significant cerebral lesions of various kinds were found in 22 of 39 cases of congenital heart disease.

Acknowledgment

The authors wish to thank Dr. Janet S. Baldwin, Department of Pediatrics, for her assistance in evaluating the clinical data.

References

1. Farre, J. R., On Malformations of Human Heart, London, Longmans, 1814, p. 24.
2. Ballet, G., Des abscès du cerveau consécutifs à certaines malformations cardiaques, Arch. gén. méd. **5**:659, 1880.
3. Abbott, Maude E., Lewis, D. S., and Beattie, W. W., Differential study of case of pulmonary stenosis of inflammatory origin (ventricular septum closed) and two cases of pulmonary stenosis and pulmonary atresia of developmental origin with associated ventricular septal defect and death from paradoxical embolism, Am. J. M. Sc. **165**:636, 1923.
4. Wechsler, I. S., and Kaplan, A., Cerebral abscess (paradoxic) accompanying congenital heart disease: Report of two cases, Arch. Int. Med. **66**:1282, 1940.
5. Hanna, R., Cerebral abscess and paradoxic embolism associated with congenital heart disease: Report of seven cases with review of literature, Am. J. Dis. Child. **62**:555, 1941.
6. Robbins, S. L., Brain abscess associated with congenital heart disease, Arch. Int. Med. **75**:279, 1945.
7. Smolik, E. A., Blattner, R. J., and Heys, F. M., Brain abscess associated with congenital heart disease: Report of case with complete recovery, J.A.M.A. **130**:145, 1946.
8. Gates, E. M., Rogers, H. M., and Edwards, J. E., Syndrome of cerebral abscess and congenital heart disease, Proc. Staff Meet., Mayo Clin. **22**:401, 1947.
9. Sweeney, D., and Patton, W., Surgical management of cerebral abscess associated with congenital heart disease, South. M. J. **43**:799, 1950.
10. Cohen, I., Bergman, P., and Malis, L., Paradoxic brain abscess in congenital heart disease, J. Neurosurg. **8**:225, 1951.
11. Abbott, Maude E., Atlas of Congenital Cardiac Disease, New York City, American Heart Association, 1936.
12. Maronde, R. F., Brain abscess in congenital heart disease, Ann. Int. Med. **33**:602, 1950.
13. Evans, W., Pathology and etiology of brain abscess, Lancet **1**:1231 and 1289, 1931.
14. Carmichael, F. A., Kernohan, J. W., and Adson, A. W., Histopathogenesis of cerebral abscess, Arch. Neurol. & Psychiat. **42**:1001, 1939.
15. Spain, D. M., and Moses, J. B., Thrombosis and embolism of pulmonary vessels with special reference to pulmonary vein thrombosis, Am. J. M. Sc. **212**:707, 1946.
16. Rich, A. R., Hitherto unrecognized tendency to development of widespread vascular obstruction in patients with congenital pulmonary stenosis (tetralogy of Fallot), Bull. Johns Hopkins Hosp. **82**:389, 1948.
17. Collis, J. L., Etiology of cerebral abscess as complication of thoracic disease, J. Thoracic Surg. **13**:445, 1944.
18. Drey, N. W., Strauss, A. E., and Gray, S. H., Functional cor biatrium triloculare, Am. Heart J. **16**:599, 1938.

19. Berthody, A., Case of communication between ventricles of heart, aorta originating from both ventricles, Med. Exam. Philadelphia NS 1:261, 1845.
20. Stone, W. H., Case of tricaelian heart with insufficiency of interventricular septum, St. Thomas's Hosp. Rep. NS 11:57, 1881.
21. Northrup, W. P., Congenital pulmonary stenosis, incompleteness of septum ventriculorum, cyanosis, abscess of brain, death at 4½ years, Arch. Pediat. 11:673, 1894.
22. Jacobi, A., Patent interventricular septum in man of 29 years, Arch. Pediat. 12:834, 1895.
23. Acker, G. N., Case of cardiac anomaly, Arch. Pediat. 12:828, 1895.
24. Deneke, T., Zur röntgendiagnostik seltenerer herzleiden, Deutsche Arch. f. klin. Med. 89:39, 1906.
25. Heigel, A., Über eine besondere form von entwicklungsstörung der trikuspidalklappe, Virchow's Arch. f. path. Anat. 214:301, 1913.
26. Raab, W., Untersuchungen über einen fall von kongenitalein herzvitium, Wien Arch. f. inn. Med. 7:367, 1923.
27. Bach, F., Case of congenital morbus cordis studied over period of twelve years, Lancet 1:1009, 1928.
28. Baumgartner, E. A., and Abbott, Maude E., Interventricular septal defect with dextraposition of aorta and dilation of pulmonary artery (Eisenmenger complex) terminating by cerebral abscess, Am. J. M. Sc. 177:639, 1929.
29. Rabinowitz, M. A., Weinstein, J., and Marcus, I., Brain abscess (paradoxical) in congenital heart disease, Am. Heart J. 7:790, 1932.
30. Ingham, D. W., Paradoxical embolism, Am. J. M. Sc. 196:201, 1938.
31. Ruhberg, G. N., Metastatic brain abscess, Minneapolis M. J. 25:108, 1942.
32. Vann, H., and Miller, E., Case of pseudo monoventricular heart terminating in brain abscesses, Anat. Rec. 88:155, 1944.
33. Sidenberg, S. S., Kessler, M. M., and Wolpaw, R., Case of tetralogy of Fallot with abscess of cerebellar vermis: Termination by brain abscess, J. Pediat. 28:719, 1946.
34. Sancetta, S. M., and Zimmerman, H. A., Congenital heart disease with septal defects in which paradoxical brain abscess causes death: Review of literature and report of two cases, Circulation 1:593, 1950.
35. Hand, A., Cerebral abscess, complication of congenital cardiac disease (tetralogy of Fallot): Report of 2 cases with diagnosis and operation, J. Pediat. 31:662, 1947.

SPANISH ABSTRACT

Abscesos Cerebrales Asociados con Cardiopatías Congénitas

Los autores sumarizan 41 casos de abscesos cerebrales asociados con cardiopatías congénitas reportados en la literatura, y describen tres casos adicionales. Se discuten los síntomas y signos de los abscesos del cerebro y acentúa especialmente la necesidad de la intervención quirurgica temprana. La ocurrencia de un dolor de cabeza persistente o letargia en un paciente con cardiopatía congénita debe investigarse mediante el exámen del líquido cefaloraquídeo, electroencefalograma y pneumoencefalograma antes de excluir completamente el diagnóstico de absceso cerebral. Se presenta la teoría de que el infarto del cerebro antecede el desarrollo de el absceso y se sugieren varios mecanismos posibles en el origen de el infarto, tales como la ocurrencia de émbolos paradoxicos, émbolo pulmonar atráves de la circulación arterial sistemica vía venas pulmonares, auricula y ventriculo izquierdo, émbolo via venas espinales, y finalmente, émbolo resultante de trombosis de las arterias cerebrales. La tendencia a el desarrollo de trombosis de pacientes con cardiopatías congénitas puede explicarse en la lentitud de la corriente sanguinea, ya bién sea debida a la presencia de policitemia o la disminución de la corriente sanguinea en la circulación pulmonar.

477 First Avenue

HYPOTONIC CEREBRAL PALSY IN MENTAL DEFECTIVES

By HERMAN YANNET, M.D., AND FRANK HORTON, M.D.
Southbury and New Haven, Conn.

SINCE mental deficiency, especially of the more severe grades, is almost invariably associated with widespread cerebral abnormalities, it is not surprising that a relatively high incidence of cerebral palsy is found among mental defectives. Thus, among the first 2000 admissions to the Southbury Training School 176 cases of cerebral palsy were encountered, an incidence of about 9%. Moreover, in children in the idiot and imbecile categories, the incidence was found to be approximately 15%.

Clinically, using the motor tone status as the differentiating factor, cerebral palsy manifests itself as either the hypertonic type, frequently referred to as "spastic" although extrapyramidal hypertonus is also included, and the hypotonic type which may vary from the most marked atonia, to barely perceptible deviations from the normal. Such associated phenomena as athetosis, tremor and ataxia may also be found in either group.

Since the classical article by Little in 1862 in which he described the "spastic rigidity of the limbs in newborn children," the literature on cerebral palsy has been almost exclusively concerned with the hypertonic group. This is not surprising since in the over-all picture of cerebral palsy, including both normal and mentally defective children, the hypertonic group is responsible for an estimated 90 to 95% of all cases. However among mental defectives, if the experience at Southbury is typical, the hypotonic group represents almost 20% of the total cerebral palsy group. Moreover, certain varieties of hypotonic cerebral palsy, namely, the atonic type, appear to be confined exclusively to the mental defective population.

It is the purpose of this paper to present a summary of findings in 31 children that compose a hypotonic cerebral palsy group.

DIAGNOSTIC CRITERIA

Unfortunately, a satisfactory and objective measure of muscle tone is not as yet available. From a practical viewpoint, however, subjective evaluation proved reasonably adequate for diagnostic classification. Actually, once the diagnosis of cerebral palsy was determined, the differentiation between the hypertonic and hypotonic varieties presented no special problem except in the presence of contractures, occasionally seen in the older hypotonic children.

The hypotonic motor defect manifests itself in three fairly distinct clinical categories, although with considerable overlapping.

1. Atonic: In these children the presenting picture is that of marked generalized atonia, hyperflexibility of joints, especially in early life, and markedly hyperactive, equal deep reflexes. In about one third of the cases the Babinski response is obtained and in a somewhat smaller number ankle clonus is present. The condition is symmetric and the

From the Southbury Training School, Southbury, Conn., and the Department of Pediatrics, Yale Medical School, New Haven, Conn.

(Received for publication July 26, 1951.)

upper and lower extremities are equally involved. An interesting observation made in almost half the cases in this group is the gradual development of flexion contractures, especially at the knees, hips, elbows and ankles, in the order given. The presence of contractures at the knees sometimes makes it difficult to elicit the usually hyperactive knee jerk. The atonic variety is the most common manifestation, 15 of the 31 children being classified in this group. Only one of these children has learned to walk and only two can sit unsupported.

2. Ataxic: This variety, which included 10 of the 31 cases shows less hypotonia and much less disability than the atonic group. All the patients could walk on admission. The gait is characterized by a wide base and gross incoordination. Variable degrees of ataxia of the upper extremities are also present. The deep reflexes are hyperactive and equal. In no case was a Babinski response or ankle clonus obtained.

3. Athetoid: This is the least common, including only six cases in this series. The hypotonia is less marked than in the first group. The athetosis is fairly typical, occasionally choreiform, involving all extremities and associated with facial grimacing. The total disability is more marked than the ataxic group but less than the atonic, since two could walk and two could sit unsupported. The deep reflexes were equal and hyperactive. Neither a Babinski response nor ankle clonus was elicited in any case.

Etiology

Efforts to establish an etiologic diagnosis were made in every case on the basis of historical data obtained from the parents, relatives, hospitals where the birth occurred, physicians caring for the child either at birth or thereafter, and from pertinent clinical and laboratory studies. As previously outlined,[1] the diagnosis of birth trauma was confined to patients with difficult or prolonged birth histories, who in addition, experienced a relatively stormy immediate postnatal period characterized by at least one or both of the following: delay in initiation of respirations, associated with continuous or intermittent cyanosis; and signs of central nervous system irritation, such as excessive drowsiness or convulsive phenomena. While it is true that some degree of brain abnormalities may stem from birth traumas not extensive enough to result in significant neonatal symptomatology, it was felt that this would probably not be the case in grossly retarded children (average I.Q. 22) with relatively devastating motor disabilities. The presence of brain abnormality related to maternal isoimmunization was investigated in all the cases where such a factor might be a possibility, by the usual blood studies in both mother and child as well as by detailed neonatal histories. Prenatal factors of admitted importance, such as maternal rubella, syphilis and toxoplasmosis, was ruled out in the usual way by detailed history, and pertinent clinical and laboratory studies. The possibility of a genetic basis for any unclassified case was entertained only in the presence of a similar neurologic and mental disorder in another sibling or close relative not explainable on another basis. It is, of course, recognized that this will overlook a variable number of genetically determined conditions not having a familial expression at the time, or perhaps resulting from mutations. Thus, the incidence for a genetic etiologic basis must be considered simply as a minimal estimate. The diagnosis of infantile central nervous system infection was accepted only in the presence of reasonable clinical and laboratory evidence at the time of the acute illness. The diagnosis of "undifferentiated" was used for those cases in which an acquired natal or postnatal condition could be ruled out, and where no recognizable prenatal causative factor could be implicated. In other words, the undiffer-

entiated group included those cases that represented congenital cerebral maldevelopment of unknown etiology. An unknown number of these are probably hereditary but cannot definitely be diagnosed as such at this time.

Table 1 summarizes the incidence of the identifiable etiologic factors in the three varieties of the hypotonic cerebral palsy group. It will be noted that all but three of the cases were due to factors that are congenital in origin. However, there is considerable variation in the relative importance of the causative mechanisms in the different clinical categories. These will be considered separately, and representative cases briefly described.

TABLE 1

HYPOTONIC CEREBRAL PALSY

Relation of Clinical Type to Etiology

Clinical Type	Total	Heredity	Infection	Birth Trauma	Kernicterus	Undiff.
Atonic	15	3		?		10
Ataxic	10	2	1		2	5
Athetoid	6	5				1
Total	31	10	1	2	2	16

ATONIC

At least three cases of the atonic group were genetically determined.

Case 1. W. E., male, was admitted to Southbury at 7 yr. of age. Although he appeared normal at birth and for the 1st 3 mo., it became apparent soon thereafter that his development was not progressing normally. At 8 mo. of age there was no evidence of significant motor development and generalized hypotonia was marked enough to be noted by the parents. Medical assistance was sought when a question of visual defect was raised. Examination at about 12 mo. revealed developmental delay, optic atrophy and retinitis pigmentosa. The subsequent development of a retro-retinal hemorrhage and glaucoma necessitated enucleation of the right eye. Histologic examination of this material in conjunction with the physical findings led to the eventual diagnosis of late infantile type of Tay-Sachs disease. The subsequent course is consistent with this diagnosis. When admitted, there was generalized hypotonia, beginning flexion contractures at both knees, markedly hyperactive deep reflexes with bilateral Babinski responses and ankle clonus. The mental status was in the idiot category. He has averaged 2 grand mal seizures per year since admission. During the subsequent 9 yr. at Southbury, there has been a slight but definite increase in the contractures which can now also be found at the elbows and ankles.

Case 2. L. J., female, was admitted to Southbury at 6 yr. of age. The early history was that of developmental delay following a normal birth and neonatal history, with a convulsive disorder, grand mal in type starting during infancy. On admission the mental status was in the idiot category and there was marked generalized hypotonia and weakness. Moderate contractures were noted at the knees, hips and ankles. The deep reflexes were hyperactive in the upper extremities but could not be elicited in the legs because of the contractures. Clinical studies were not contributory as regards etiologic diagnosis. At 10 yr. of age, a repeat skull RG showed beginning intracranial calcification, and at about the same time, small adenoma sebaceum were noted at the nasolabial folds. A pneumoencephalogram showed the characteristic tuberosities projecting into the lateral ventricles, and confirmed the diagnosis of tuberous sclerosis.

Case 3. J. B., male, was admitted to Southbury at 6 yr. of age. Past history was that of a normal pregnancy, birth and neonatal period. Developmental delay was obvious early, and grand mal convulsions began at 8 mo. of age and have continued. On admission to Southbury at 6 yr. of age, there was marked hypotonia and weakness with hyperactive deep reflexes but no contractures. Etiologic

studies were not contributory. Repeat skull RGs at 11 yr. of age revealed intracranial calcification and at about the same time adenoma sebaceum appeared at the nasolabial folds leading to a diagnosis of tuberous sclerosis. During the following 2 yr. beginning contractures were noted at the knees. The boy walks poorly without evidence of significant ataxia. His mental status is in the idiot category.

Comment: These three cases have in common the fact that during early life they presented a typical picture, neurologically, of the atonic type of cerebral palsy. Within variable periods other manifestations appeared leading to the etiologic diagnosis of late infantile Tay-Sach's disease in the first case, and tuberous sclerosis in the other two cases. Both conditions are genetically determined, the former being recessive in character, the latter, dominant. Although these are pathologically entirely separate and distinct entities, they do have in common the fact that the pathologic abnormality is generalized throughout the brain with associated severe ganglion cell disturbance. That other types of degenerative conditions or dysplasias with extensive ganglion cell involvement may occasionally produce the clinical picture of atonic cerebral palsy is likely.

The next two cases exhibit an entirely different etiologic mechanism, namely, extensive cerebral damage sustained during birth. One of these will be described.

Case 4. L. B., male, was admitted to Southbury at 6 yr. of age. Family history was noncontributory and pregnancy uneventful. Delivery was prolonged and difficult, and a diagnosis of severe cranial trauma was made at delivery. This was confirmed by the clinical and laboratory findings during the neonatal period, which was stormy and associated with episodes of respiratory difficulty and twitching. The baby was given transfusions twice, and remained in the hospital for a considerable period. At 6 mo. of age he developed generalized convulsions, more marked on the left. A pneumoencephalogram done soon after, showed cortical atrophy with some enlargement of the ventricles, especially on the right. There was little evidence of subsequent developmental progress. On admission to Southbury at 6 yr. of age, the mental status was in the idiot category and there was generalized hypotonia with markedly hyperactive deep reflexes, bilateral ankle clonus but without Babinski responses. During the subsequent 7 yr., the child developed mild contractures at the knees, but was able to sit unsupported. The hypotonia became less marked. The convulsive disorder, as previously described persisted, although reasonably well controlled by medication.

The remaining 10 cases in the atonic group were unquestionably congenitally determined, although no recognizable etiologic factor could be implicated. The possibility of these being due to an identical single specific recessive genetic factor seems unlikely. In these 10 families there were available records of 24 other siblings, all of whom are entirely well. Neither could any pertinent findings in the parents or collaterals be elicited. There was no evidence of consanguinity in the parental histories.

Ataxic

Of the 10 cases with ataxia as the primary defect, two were in siblings and were presumably of hereditary etiology. Another child sustained cerebral damage as a result of infantile encephalitis, and is described below:

Case 5. J. F., female, was admitted to Southbury at 4 yr. of age. Family history and past history were not contributory. The child was entirely well in every respect until 10 mo. of age when she developed rubeola. On the third day CNS symptoms and physical findings led to the diagnosis of postmeasles encephalitis, and the child was hospitalized. Improvement was gradual but never complete. On admission to Southbury the mental age was estimated at 1 yr. There was marked ataxia of the lower extremities, less so of the trunk and upper extremities. The muscle tone was significantly hypotonic and the deep reflexes were hyperactive, more so on the right. The weakness, although generalized, was also somewhat more marked on the right. At present she walks with a wide base and ataxic gait. She is also unsteady when sitting. There has been only slight growth in mental status, and her present developmental quotient is estimated at 30%.

Two children in this group were diagnosed as probably examples of kernicterus. The term "kernicterus" is used in the broadest clinical sense to include cases of cerebral pathology most often seen as a complication of erythroblastosis fetalis but also encountered following a wide variety of neonatal illnesses, especially in premature infants, characterized frequently by severe or prolonged jaundice.[2-4] One of these cases has previously been reported.[3] It will be briefly summarized in order to bring it up to date.

Case 6. T. W., male, was admitted to Southbury at 5 yr. of age. There were 2 normal older siblings. He was the third of 5 pregnancies. The fourth and fifth were stillborn. The mother was Rh-negative and the patient Rh-positive. The neonatal period was characterized by severe jaundice and a fairly typical picture of erythroblastosis fetalis, requiring repeated transfusions. The subsequent course was that of delayed development in all spheres. On admission to Southbury, his mental age was estimated at 2 yr. There was moderate hypotonia and gross generalized ataxia, more marked in the lower extremities. His gait was unsteady with repeated falls. In the ensuing years, his motor progress has been decidedly above his intellectual growth. His ataxia, although still present, is much less evident and much less incapacitating. He walks reasonably well and can partake of the usual activities compatible with his mental status which continues to be estimated at an I.Q. level of 40.

The next case with ataxia is also considered an example of "kernicterus" although not related to Rh isoimmunization.

Case 7. D. M., male, was admitted to Southbury at 7 yr. of age. Family history was not contributory. There is one younger sibling who is well. The year following admission, the mother was studied in detail by the authors as regards possible isoimmunization, with negative results. The child was born following an uneventful pregnancy, delivery was normal. Birth weight was barely 2.7 kg. On the second day severe jaundice gradually appeared and persisted for almost 2 mo. This period was extremely stormy according to the hospital records, requiring frequent transfusions. There was no mention of blood culture to rule out sepsis. Convulsions were also noted during this period but none occurred subsequently. At home, his development was delayed in all spheres. On admission to Southbury his mental status was in the idiot category. There was generalized ataxia and moderate hypotonia. The deep reflexes were equal and hyperactive without Babinski responses, but with bilateral ankle clonus. The gait was similar to Case 6, being grossly unsteady with many falls. During the next 8 yr., there has been significant improvement in the gait, although this is still on a wide base. The ataxia and hypotonia are less evident, and there are no contractures. The mental status, however, continues in the idiot range.

Comment: The similarity in neonatal history, clinical course, findings and outcome make it likely that both these cases are related to cerebral lesions associated with neonatal jaundice, although of different etiologic mechanisms.

The remaining five cases in the ataxic group were congenital in nature without recognizable etiology.

Athetoid

Of the six cases in the athetoid group, five were definitely hereditary in nature. All these children had siblings with a strikingly similar neurologic picture and mental status although occasionally with some variability in degree of severity. The possibility that the sixth case also represents a genetic condition cannot be ruled out since there is only one other sibling who is normal, and no other etiologic factors could be elicited.

In summary, as regards causation, of the total group of 31 cases, almost one third was definitely hereditary, and an additional one half was congenital in nature but of unknown etiology, while the remaining one sixth was distributed among postnatal conditions such as birth trauma, cerebral inflammation and cerebral lesions associated with severe neonatal jaundice of variable cause.

Additional Clinical Features

The average age of the children with hypotonic cerebral palsy on admission to the school was 8.7 years, while the average period of observation was 7.3 years. The mental deficiency was most marked in the atonic (av. I.Q. 15) and athetoid (av. I.Q. 20) groups, although the ataxic group also showed serious retardation (av. I.Q. 35). Microcephaly occurred frequently in all three groups but was most frequent in the atonic category. The average head circumferences and their ranges were as follows: atonic, av. 47.5 cm. (range 43-52); athetoid, av. 48.2 cm. (range 41-51); ataxic, av. 52.0 cm. (range 49-56). Convulsive disorders were frequent, occurring in almost 50% of the atonic, 30% of the athetoid and 10% of the ataxic groups. The clinical manifestations were primarily of the grand mal variety at the time of admission. In most of the cases the onset of spells was during the first year of life, rarely after the third year. In two children of the atonic group, mass myoclonus was present from early infancy until the end of the second year when grand mal manifestations appeared. In one child of the ataxic group, the akinetic type of petit mal was described during the early years but was not present on admission at 5 years of age. Contractures, as previously described, were found most often in the atonic (50%) and athetoid groups (30%) but in none of the ataxic group. Nystagmus was noted in four of the total series. Three occurred in the ataxic group and one in the athetoid. Except for the patient with Tay-Sach's disease, the fundoscopic examinations revealed no abnormal retinal or optic disc changes in any of the cases.

Pneumoencephalograms were carried out in four children in the atonic group. All were interpreted as indicating extensive cortical atrophy. In two cases, in addition, the lateral ventricles appeared somewhat enlarged. One child in the ataxic group showed similar findings. One child in the athetoid group, studied early in life, had what was considered a normal pneumoencephalogram.

An interesting feature in these hypotonic children of all types is the tendency for the hypotonia to become less demonstrable as the child grows. This is most evident in the atonic group, presumably because of the more severe original hypotonic state. There is also the impression that the motor power also tends to improve under these conditions, although to a limited degree.

Discussion

Each of the three varieties of the hypotonic type of cerebral palsy has been previously described, although in limited fashion. In 1909, Foerster[5] first reported what has since been known as the atonic type of cerebral diplegia, or more recently, congenital atonic diplegia. The gross appearance of the brain in two cases was also described by Foerster as showing atrophy of the frontal lobes without gross evidence of cerebellar abnormality. Clinically, his patients were all mentally retarded, with marked hypotonia, hyperactive deep reflexes and normal muscle electric reactions. It is of interest that "Foerster's symptom" was not noted in any of the cases reported here, presumably because of the older age at which the children were first seen. This symptom manifests itself by the disappearance of the marked atonia of the lower extremities which become drawn up when the infant is supported in the upright position at the arm pits. Batten and von Wyss described four cases of atonic diplegia.[6] Two of these were said to have shown some hypertonus during the course of their disease. It is interesting to speculate as to

whether this so-called "hypertonus" might not be evidence of contractures that occur so frequently in these cases and may be confused with spasticity. Isolated cases have also been described by others.[7-11] Brandt[7] has recently called attention to cases of the atonic type, stressing the variable etiology and indicating the frequent diagnostic confusion that may occur with cases of amyotonia congenita or progressive infantile muscular atrophy.

Up to the present, all the reported cases of atonic diplegia have been in children with marked degrees of mental retardation. This agrees with the authors' experience at Southbury as well as with the extra-institutional contacts with a wide variety of pediatric neurologic patients. Although available pathologic studies of this syndrome are too meager to warrant a definitive statement, it may be reasonable to assume that the extent of cortical involvement necessarily associated with this variety of hypotonic cerebral palsy makes it likely that normal or even borderline intellectual functioning would not be compatible with this type of neurologic abnormality.

Seven of these 10 cases of the ataxic group would fit in the well recognized diagnostic category of congenital cerebellar ataxia insofar as neurologic features are concerned, as described by Ford.[11] As he indicates, however, here the mental development is, as a rule, quite normal. That the pathology in the present authors' cases is much more extensive, involving the cerebrum as well as the cerebellum and associated tracts, must be assumed.

As indicated above, the occurrence of variable degrees of contractures, especially in the atonic group, is a relatively common observation in the older child. The mechanism has not been established. A possible explanation may be a variable growth differential between the long bones and the imperfectly ennervated muscle groups, especially the flexors, resulting in significant relative shortening of the latter. In favor of this view are the observations indicating the absence of contractures in the very young infant, its gradual development during the period of rapid growth and the tendency to reach a variable degree of severity which tends to remain fairly stationary in the postpuberal period. Because of the long period during which the tendency towards contractures remains active, prophylactic efforts present a most difficult and discouraging problem. The marked intellectual defect, and the severe motor handicap make the prognosis for future serviceable ambulation extremely poor for most of the atonic group. From a practical viewpoint, since it is in this group that the incidence and severity of the contractures are greatest, the relative difficulties of preventing or minimizing the disfiguring contractures complicates only slightly the over-all problem of bed care which most of these children require.

Summary

The relative importance of the hypotonic type of cerebral palsy among the mentally defective is stressed. This type of cerebral palsy manifests itself in either of three clinical pictures with some overlapping, namely, atonic, ataxic and athetoid. The etiology is variable in each of these groups and may be effective in either the prenatal, paranatal or postnatal periods.

The severity of the mental defect, the high incidence of convulsive disorders, and the tendency toward microcephaly point towards the widespread nature of the pathologic process regardless of etiology.

The syndrome of atonic diplegia, as herein described, is probably invariably associated with the more severe degrees of mental deficiency.

References

1. Yannet, H., Infantile cerebral palsy cases with severe mental deficiency, PEDIATRICS **3**:820, 1949.
2. Aidin, R., Corner, B., and Tovey, G., Kernicterus and prematurity, Lancet **2**:1153, 1950.
3. Yannet, H., and Lieberman, R., Central nervous system complications associated with kernicterus, J.A.M.A. **130**:335, 1946.
4. Zuelzer, W. W., and Mudgett, Roxie T., Kernicterus, PEDIATRICS **6**:452, 1950.
5. Foerster, O., Atonic-astatic type of infantile cerebral palsy, Deutsche Arch. f. klin. Med. **98**:216, 1909.
6. Batten, F. E., and von Wyss, W. H., Atonic form of cerebral diplegia, Brit. J. Child. Dis. **12**: 65, 1915.
7. Brandt, S., Werdnig-Hoffman's Infantile Progressive Muscular Atrophy, Copenhagen, Ejnar Munksgaard, 1950, p. 236.
8. Clark, I. P., Infantile cerebro-cerebellar diplegia of flaccid, atonic-astatic type, Am. J. Dis. Child. **5**:425, 1912.
9. Davison, C., and Weiss, M. M., Muscular hypotonia associated with congenital heart disease, Am. J. Dis. Child. **37**:359, 1929.
10. Fearnsides, E. G., Case of atonic form of cerebral diplegia, Brit. J. Child. Dis. **12**:166, 1915.
11. Ford, F. R., Diseases of Nervous System in Infancy, Childhood and Adolescence, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1945, pp. 208, 215 and 217.

Spanish Abstract

Parálisis Hipotonicas de Origen Cerebral en Niños con Deficiencia Mental

Los autores destacan la importancia relativa de las parálisis hipotonicas de origen cerebral en niños con deficiencia mental. Esta condición se manifiesta especialmente en aquellos casos severos de deficiencia mental, en los cuales, de acuerdo con la experiencia de los autores puede alcanzar una incidencia cercana a un 20% del grupo total de las parálisis de origen cerebral. Clinicamente, esta variedad de parálisis se manifiesta en tres formas clinicas distintas, aunque un número considerable de formas mixtas pueden ocurrir. Estas formas son: la forma atonica, la forma ataxica y las formas atetoides. La patogénesis de esta condición es variable incluyendo factores géneticos, condiciones prenatales de naturaleza diversa, traumatismos en el parto, kernicterus secundario a isoinmunización ú otro mecanismo, encefalopatías inflamatorias infantiles y también enfermedades degenerativas. A pesar, que solo unas pocas descripciones patologicas de esta condición han sido reportadas, puede asumirse, basandose en la severidad del defecto mental, en la gran incidencia de los trastornos convulsivos y en la tendencia a la microefalia, qué los cambios en el cerebro son de naturaleza generalizada y extensivos sea quién fuera el factor etiológico.

Southbury Training School

FURTHER STUDIES ON THE INFLUENCE OF HISTAMINE ON PLATELET ACTIVITY, WITH ESPECIAL REFERENCE TO ITS ACTION ON THE BLOOD OF THE HEMOPHILIAC PATIENT

By HEYWORTH N. SANFORD, M.D., F. RICHARD HALL, M.D., AND STUYVESANT BUTLER, M.D.
Chicago

THE use of intravenous injections of histamine in the treatment of hemophiliac patients was reported by the authors in 1948.[1] At this time it was not possible to state the exact mechanism of this reaction, as the various phases of the problem were under study. This paper is a report of further work in this problem, as well as the results obtained in the continued treatment of hemophiliac boys by this method.

The work was initiated by a study of the blood of 15 patients suffering from migraine, whose blood did not deviate in any manner before injection with the histamine from that of normal individuals. It was observed that during the intravenous injections of the histamine the qualitative platelet activity of their blood was increased.[2] Since this work was published, 80 additional individuals have been studied in a similar manner using the technic of Sanford and Leslie.[3] In no instance was there any change in the total number of circulating platelets either during or following the histamine injections.

There was however a small but constant decrease in the coagulation times of the whole blood, and both plasma fractions, which was interpreted as an increase in the qualitative activity of the platelets, possibly related to an increased disintegrative rate with a release of thromboplastic material. In this study it was found that following injection of histamine, the average decrease in the coagulation time of the whole blood was 12.6%, of normal plasma (plasma A) 7.25% and platelet-free plasma (plasma B) 7.58%. These are shown graphically in chart 1.

Having shown clinically that when histamine was injected intravenously it hastened the disintegration of the platelets, the following studies were made in an attempt to find the mode of action of histamine on this platelet activity or disintegration.

EXPERIMENTAL STUDIES

In Vitro Action: The first investigation was to study the possibility that the entire phenomenon might be on a direct action basis. If this were true the action of histamine on normal platelets should occur equally in vitro as in vivo. Comparisons were made on the blood of five normal individuals and seven dogs adding 0.055% of histamine to the plasma A of each, and comparing similar plasma A without the histamine, but with 0.9% normal saline added. These comparisons were made by direct observation and by photomicrographs. No difference was noted in any instance between the histamine-

From the Department of Pediatrics and Medicine, Presbyterian Hospital, University of Illinois Medical School, Chicago.

Supported by grants from the Otho S. A. Sprague Fund, Mrs. Louise DeKoven Bowen and Abbott Research Laboratories.

(Received for publication Aug. 29, 1951.)

treated specimens and the normal saline solutions. It can be said therefore that histamine has absolutely no action in any way on the blood platelets of the dog or human in vitro.

In Vitro Action of Intravenous Histamine: After centrifugation at 2200 rpm for 90 seconds, portions of the platelet containing supernatant plasma (plasma A) were mixed with an excess of heparin and placed on a chilled counting chamber from which the air was excluded by a wax seal. Photomicrographs were taken with high dry magnification

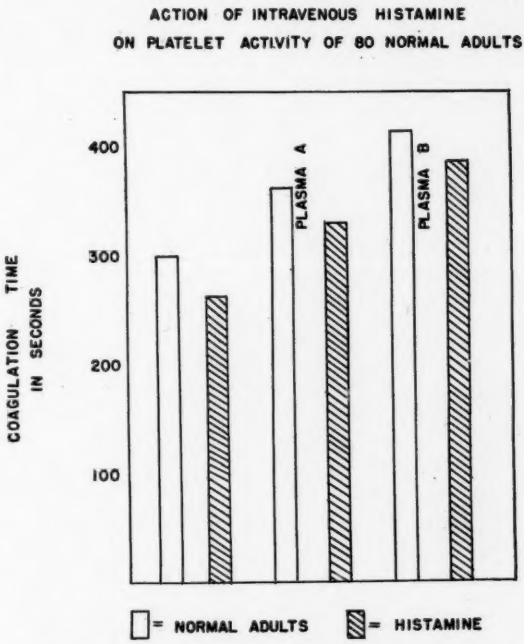


CHART 1. First 2 columns show average decrease of coagulation time of whole blood 12.6% following intravenous injections of histamine; following these are platelet-rich plasma (plasma A) 7.25% and platelet-free plasma (plasma B) 7.58%.

every three minutes for an hour.[4] It was found that the platelets of a normal human being could be preserved at room temperature without clumping or disintegration for many hours. However, during the intravenous administration of histamine the platelets clumped together and seemed to disintegrate more rapidly. This increase in the rapidity of clumping seemed to be related directly to the degree of reaction the patient experienced from the infusion.

Another series of observations were made comparing the behavior of normal platelet preparations with and without heparin as an anticoagulant, with preparations that were made during intravenous histamine administration. It was observed, as has been known for many years, that heparin preserves the integrity of the normal platelets, and that without heparin they will clump and disintegrate rapidly. However, the authors observed that after the administration of intravenous histamine to a normal individual whose

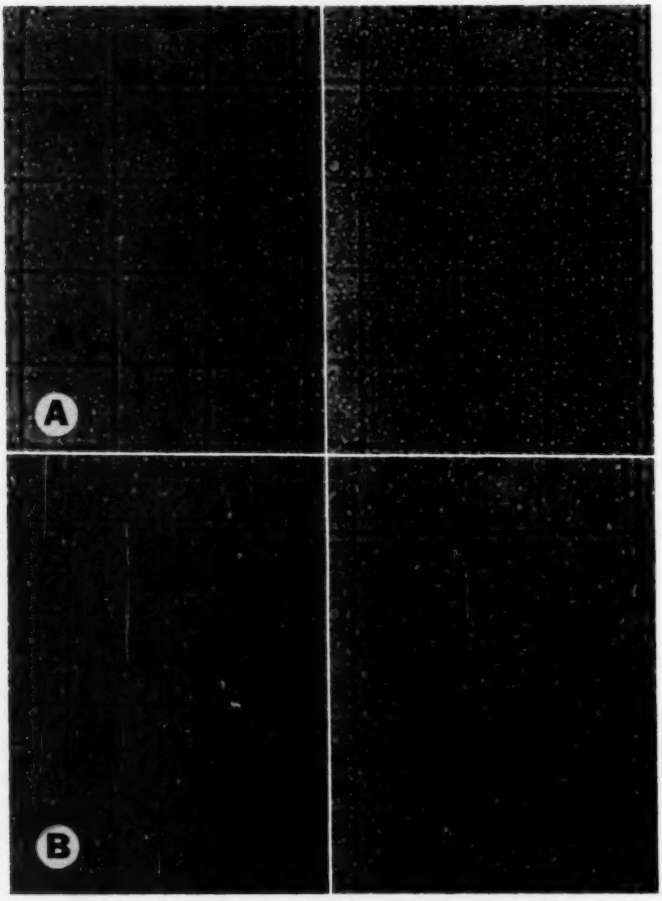


FIG. 1. Serial photomicrographs (x 440) showing action of blood platelets in normal individual following preservation with heparin and after injection of histamine. A. Left, 1 min.; right, 60 min. Platelets from normal individual preserved with heparin. Note that there is no change in 60 min. B. Left, 1 min.; right, 60 min. Platelets from normal individual after injection with histamine. Note that even when preserved with heparin, there is beginning clumping and agglutination.

platelets had previously been well preserved with heparin, no excess of heparin would now counteract the increased agglutinative and disintegrative tendencies produced by the histamine (Fig. 1).

Animal Experiments with Massive Injections of Histamine: Inasmuch as these experiments indicated that the rapidity of clumping and disintegration of the platelets might be directly proportional to the degree of reaction of the patient, the following studies were made using massive doses of histamine in animals, such as are not possible in the human subject.

Twelve dogs were used in this experiment. Three were used for controls. Three were given histamine 0.06 mg./kg., three were given histamine 0.60 mg./kg. and three histamine 6.0 mg./kg.[5] The results (see chart 2) show a definite increased speed of coagulation in all three blood fractions. Whole blood clotting time is decreased from an average of 292 seconds to an average of 246 seconds, platelet-rich plasma (plasma A) from an average of 270 seconds to an average of 228 seconds, and platelet-free plasma (plasma B) from an average of 267 seconds to an average of 213 seconds. Little change in the number of platelets between the control dogs and those receiving human therapeutic doses (164,000 and 160,000) was observed. However, with the massive doses the platelet counts drop first to 149,000 and then to 101,000.

Further Clinical Observations on the Use of Histamine in Hemophilia: The use of

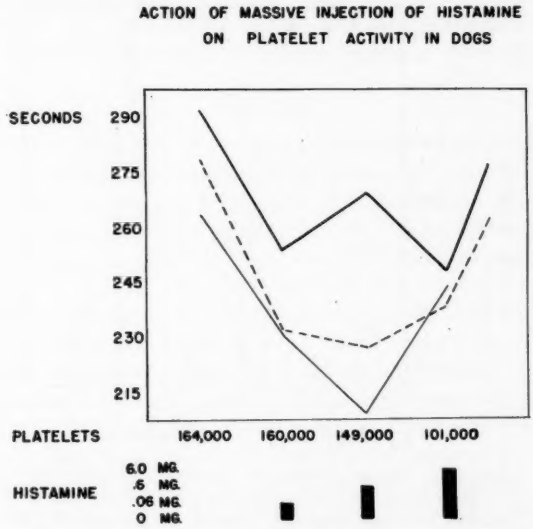


CHART 2. Average changes in quantitative and qualitative platelet activity in 12 dogs following massive injections of histamine. Coagulation time of whole blood is shown by heavy line, platelet-rich plasma (plasma A) by dotted line, and platelet-free plasma (plasma B) by lighter line.

intravenous injections of histamine in the treatment of hemophiliac patients was begun by the authors in 1947. In the original report five boys have been treated by this method over a period of two years. Three years later of the original five, two have died, one from lobar pneumonia, and one from encephalitis following epidemic parotitis. While there were no associated hemorrhagic manifestations that could in any way be related to these deaths, they showed a lack of resistance far below that which might be expected in normal boys of that age. The remaining boys show improvement over their former status, with bleeding cycles that are much shorter, and with considerate increase over their former intervals between cycles. They are living fairly adequate lives.

Since this report the authors have treated 11 more boys at the Presbyterian Hospital and the Cook County Hospital, and have received reports of six more in which this

treatment had been used throughout the country. Of these reports five showed results in shortening the bleeding cycle, and one was a complete failure. One usually hears of the good results, and seldom of the failures; there may have occurred more poor results than have so far been reported. In this series nine have shown a consistent decrease in their bleeding cycles; two showed no results at all and transfusions were necessary (chart 3). All these boys continue to have active bleeding but, as in the first series, the cycles are shorter and the interval between active cycles is appreciably longer.

In all the patients there has been a tendency for the condition to be more refractory

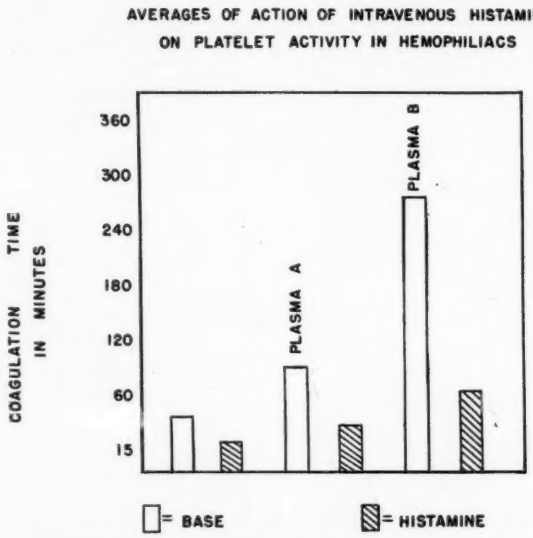


CHART 3. Average changes in qualitative platelet activity of 22 hemophiliac boys following injections of histamine. First 2 columns are coagulation time of whole blood; following are platelet-rich plasma (plasma A) and platelet-free plasma (plasma B). In 3 of the boys no results were obtained.

as the treatments are continued. That is, with each bleeding cycle the histamine takes a longer time to cause the blood coagulation to decrease to the base line for that individual. In one of the older boys given treatment during a bleeding cycle, the improvement in coagulation, which had formerly occurred during the first or second injections, did not occur till the fifth injection. He was about to be discharged when he began to have hematuria. This was not lessened by continued administration of histamine, and it was necessary to give him two blood transfusions.

In these individuals who have received injections several times, it was found preferable to give these injections during a quiescent period between cycles. This serves to extend the nonbleeding cycle for some time. In some instances the histamine was given daily for 20 days instead of the usual five days. This seems to considerably lengthen the quiescent period.

In some instances in the older boys who have had considerable treatment, the amount

of histamine was increased to as high as 3.0 mg. instead of the usual end level of 1.0 mg. This seems to make very little difference and serves chiefly to give more histamine reactions as shown by flushing of the skin and headaches. This to a small degree shows clinically the same results that were obtained in experimental high levels in dogs. It has also been found that the infusions can be given just as well by hypodermoclysis as by intravenous injections. The former method, in which the drug is given at a rate of about 10 drops per minute, requires several hours. Hypodermoclysis saves considerable time and extra hospital expense and seems to cause no untoward reactions.

The following plan has been followed in the administration of the histamine to hemophiliac patients: histamine 0.1 mg. is given the first day, 0.2 mg. the second, 0.4 mg. the third, 0.8 mg. the fourth and 1.0 mg. the fifth day. The amount of histamine is not increased above 1.0 mg. even in a longer series. By intravenous injection the histamine is given in 250 cc. of isotonic sodium chloride solution at a rate of 20 drops per minute. By hyperdomoclysis the same quantity is given at the rate of 10 drops per minute.

Discussion

In the problem of attempting to discover the action of histamine on the blood platelets, it seems obvious from these experiments that the total quantity or number of the blood platelets is in no way affected by the histamine until shock levels are reached. One explanation for the unchanged platelet quantity in these human subjects, with an increase in the speed of coagulation of whole blood and both plasma fractions, is that an increased destruction of platelets with increased qualitative activity was matched by increased production or release of platelets from storage depots. Still higher levels of histamine such as are presumably found in shock should logically accelerate still further their disintegration, and their total number would actually decrease.

It has been recognized for some time that during peptone and anaphylactic shock and in thrombocytic purpura simultaneous clumping out of platelets and vasodilation occur. Theoretically, since platelets are no longer available for the removal of free histamine from the blood, this free histamine might well be the cause of the vasodilation. Of course many different mechanisms are operating in clinical shock, but histamine is certainly one factor. Therefore if a shocklike state might be achieved by histamine the total number of platelets should decrease. This could only be demonstrated experimentally in animals with one hundred times the concentration of histamine necessary to reduce the coagulation time of the blood to approximately the same value as was achieved without shock with smaller concentrations.

To put this in another way, with one hundred times the concentration of histamine necessary to reduce the coagulation time of the blood to its lowest value, it was possible to reduce the total platelet quantity in animals about 30%, but with no more change in the qualitative action of their platelets then could be induced by one hundredth of this quantity of histamine. This reduction amounted to approximately 12%. Intravenous injections of histamine do not alter the total quantity of the blood platelets except in shock concentration, and this reduction does not materially affect the already decreased blood coagulation time.

These studies have demonstrated that histamine definitely alters the qualitative activity of the blood platelets. This increase in rapidity of clumping seems to be related directly to the degree of reaction the patient experiences from the infusion. As it does not take

place in vitro, there is certainly no direct action or injury to the platelets themselves. However, inasmuch as clumping of the platelets is a forerunner of their disintegration, and inasmuch as in vitro the platelets are not freely movable as in the blood stream, it is not known if there is interference with whatever force is necessary to draw the platelets together in preparation for agglutination. Since this attraction is not understood, to postulate this action as caused by electric charges or some chemical affinity is beside the point. The authors have been unable to prove or disprove the possibility of such a reaction.

It is obvious that the histamine must cause changes in other tissues or circulating substances of the body besides the platelets. The authors at one time postulated that these changes might be on new platelets forming in the hematopoietic system. This is now doubtful as these changes occur too soon for any such new platelets to definitely influence the coagulation equilibrium. In a patient whose platelets had previously been well preserved with heparin, the authors found that following the administration of intravenous histamine, no excess of heparin would counteract the increased agglutinative and disintegrative tendencies produced by histamine.

This evidence would seem to show that heparin and histamine have some antagonistic action on platelet activity; histamine may therefore have the power to bind heparin or at least limit its activity as a protector of platelet disintegration in the blood stream. It also raises the question whether histamine is not itself actually, or if not, at any rate increases the production of, the thrombocytolysin described by Brinkhous.[6] This substance, he believes, acts on the platelets, causing them to clump, break down and liberate their thromboplastin content.

Conclusions

Clinically and experimentally intravenous and subcutaneous injections of histamine increase directly the qualitative disintegrative ability of the blood platelets. It has no effect on the total platelet count (quantitative action) until shocklike levels are obtained. It then causes a decrease in the number of the circulating platelets in the blood.

This qualitative action may be in part due to an antagonistic action between heparin and histamine. Heparin in high concentrations does not inhibit completely the increased tendency toward in vitro agglutination of the platelets exposed in vivo to histamine.

In 22 hemophiliac boys, intravenous and subcutaneous injections of histamine decreased the coagulation time of the blood by increasing the platelet disintegration in 19 patients. It was a complete failure in three of the boys. The action of the histamine is not permanent, and tends to become less efficient as more injections are given. However, it is sufficient to cause a cessation of bleeding and to decrease the coagulation time of the blood to its normal value for that person in the majority of instances.

Acknowledgment

The authors are indebted to Mr. Norman Piercy for the design and construction of special equipment used in this work.

References

1. Sanford, H. N., Butler, S., and Kennedy, S. R., Action of intravenous histamine on blood of hemophilic child, Am. J. Dis. Child. **76**:6, 1948.
2. Butler, S., Thomas, W. A., and Sanford, H. N., Blood coagulation during intravenous injections of histamine, J. Lab. & Clin. Med. **32**:1432, 1947.

3. Sanford, H. N., and Leslie, E. I., Improved method for estimation of qualitative and quantitative platelet factors, J. Lab. & Clin. Med. **27**:255, 1941.
4. Hall, F. R., and Butler, S., Observations of character of platelets studied with new photographic technique, J. Lab. & Clin. Med. **34**:1604, 1949.
5. Butler, S., Hall, F. R., and Sanford, H. N., Observations on influence of intravenous histamine on qualitative platelet activity, J. Lab. & Clin. Med. **36**:710, 1951.
6. Brinkhous, K. M., Clotting defect in hemophilia: Deficiency in plasma factor required for platelet utilization, Proc. Soc. Exper. Biol. & Med. **66**:117, 1947.

SPANISH ABSTRACT

Estudio de la Influencia de la Histamina Sobre la Actividad Cualitativa de las Plaquetas, con Referencia Especial a su Acción Sobre la Sangre de Pacientes con Hemofilia

Estudios clinicos y experimentales realizados por los autores demostraron que la administración intravenosa o subcútanea de histamina incrementa la propiedad cualitativa de desintegración de las plaquetas. El conteó total de plaquetas (acción cuantitativa) no fué afectado hasta que los niveles de histamina obtenidos producían colapso general (shock), observandose entonces una disminución del número total de las plaquetas circulantes.

Esta acción cualitatitiva puede ser debida en parte a la acción antagonista entre la heparina y la histamina. Concentraciones elevadas de heparina no inhiben completamente la tendencia marcada hacia la aglutinación "in vitro" de las plaquetas expuestas a la histamina "in vivo."

En la administración de la histamina a pacientes con hemofilia el siguiente plan fué seguido: 0.1 mg. el primer día, 0.2 mg. el segundo día, 0.4 mg. el tercero, 0.8 mg. el cuarto y 1.0 mg. el quinto día. Si se desea una serie mas larga, la cantidad de histamina no debe aumentarse por arriba de 1.0 mg. por dósis. La histamina puede administrarse intravenosamente en 250 cc. de solución isotonica de cloruro de sodio a una velocidad de 20 gotas por minutos. La misma cantidad puede administrarse por hipodermoclisis a una velocidad de 10 gotas por minuto.

En 22 niños hemofilicos este tratamiento disminuyó el tiempo de coagulación de la sangre (mediante al aumento de la desintegración de las plaquetas) en 19 de los casos. En tres pacientes no se observó efecto alguno. Esta acción de la histamina no es permanente y tiende a perder su eficacia con el uso repetido. Sin embargo su acción es suficiente para producir la cesación del sangramiento y la disminución del tiempo de coagulación de la sangre a los valores normales en la mayoria de los casos.

952 North Michigan Avenue

LOCALIZED HYPERTROPHIC EMPHYSEMA

By ROBERT R. SHAW, M.D.
Dallas

LOCALIZED emphysema involving a segment of a lobe or a whole lobe which is not associated with an aspirated foreign body or tenacious mucus of an upper respiratory infection is a rare condition which has received little attention in the literature. It is important that it be diagnosed early in infancy since early surgical removal of the involved pulmonary tissue will improve the respiration of the infant and prevent deformity of the chest. The first report of this condition was by Leahy and Butsch.[1] It appeared as a case report in a paper entitled "Surgical Management of Respiratory Emergencies During the First Few Weeks of Life." In an excellent discussion of this condition, they reviewed the literature of associated emphysematous states in infants and children. They were able to find one isolated case report by Royes[2] who described what he called "localized hypertrophic emphysema" in the middle lobe of a 28 year old male. This finding was made at a postmortem examination following a fatal accident. The description of Royes of the finding in his case seems similar to the findings in the cases being considered in this report, although his theory as to the etiology of this condition could not be confirmed by the findings in the patients reported here.

Localized pulmonary distention in infants and children is not an unusual finding. These areas of distention are usually intermingled with areas of patchy atelectasis as the result of obstruction of the smaller bronchi by thick viscid muscus. In some bronchi the block is complete while in other bronchi there is a ball valve action which allows segments of the lung to become over-distended by trapped air. This type of emphysema has been described frequently in the literature. Caffey[3] described regional obstructive pulmonary emphysema in infants and children. He reported seven cases all associated with acute respiratory infections. The cystic dilatations could be seen on the roentgenograms of the chest. In all these patients the condition was a transient one, and the appearance of the lungs returned to normal with nonoperative treatment. Obstructive emphysema of a lung or a lobe is a common occurrence with aspirated foreign bodies in infants and children.

Localized hypertrophic emphysema is a pathologic entity affecting a segment or a lobe of a lung. In the four patients that the author has seen with this condition, all other segments of the lung were entirely normal. The diseased segment is enlarged to many times its normal volume in a uniform dilatation of the air sacs. The bronchi, arteries and veins are much smaller than one would expect to find supplying a segment of lung. Even when the bronchi are opened and the segment of lung tissue is removed from the body it does not collapse appreciably. It is uniformly pink in color even in adults, indicating that it has not taken part in the usual ventilation of normal lung tissue. Except for its pink color, it more closely resembles gelfoam than any other substance. Several hours after being removed from the body, this tissue will float upon water with less than a tenth of its volume being submerged. Microscopic examination of the tissue reveals air sacs

From the Department of Surgery, Southwestern Medical College of the University of Texas, Dallas.

(Received for publication Sept. 11, 1951.)

and alveoli that are generally distended and empty. The intervening septae are thin and there is no inflammatory reaction. The blood vessels are small and have thin walls. The bronchioles are empty. The bronchial mucosa is normal except for slight chronic inflammatory infiltration. The cause of the emphysema is not evident in the examination of the specimens.

There seems to be ample evidence to consider this pathologic entity as having a congenital etiology. The two patients in the present report were known to have the condition as early as two weeks following birth. In the two adults seen with this condition the history suggests that the condition was present probably all of their lives. Since the only possible treatment for his condition is surgical excision of the involved segment of lobe, it is important that it be recognized.

The following cases are reported to illustrate the diagnostic and therapeutic problems presented by this type of emphysema.

Case Reports

Case 1: A 4 yr. old boy was first seen in the office. History revealed that a roentgenogram (Fig. 1 A) had been taken of his chest at the age of 2 wk. because of a wheezing type of respiration. The roentgenogram having suggested a large thymus gland, roentgen therapy was given over the mediastinum. Following this the wheezing respiration disappeared, but the child gradually developed a severe pectus excavatum. RG taken at the age of 2 wk. also revealed an area of translucency in the upper part of the left lung field. This was overlooked at that time. Two years following birth another RG (Fig. 1 B) was taken which revealed this same area of translucency. The area of the translucency had increased in size in proportion to the increase in the size of the child. Four years following birth RGs (Fig. 1 C) were again taken of the chest and revealed the same findings. The appearance was much like that of a pneumothorax except that fine shadows indicating trabeculae could be seen running through the area of decreased density. A bronchogram was done which showed that the bronchi of the left lung were crowded into the inferior medial portion of the left hemithorax. No oil entered the bronchi leading into the emphysematous portion of the lung.

Eleven days after the patient was first seen by the author, the left chest was opened through the fifth rib bed. Upon opening the pleural cavity an emphysematous left upper lobe bulged out of the incision. The major portion of this lobe was made up of a localized emphysema. In this emphysematous area all resemblance of lobular structure was absent. The small arteries and veins were divided. These vessels seemed to be almost bloodless. The bronchus to the emphysematous area was then isolated and divided and the proximal bronchus closed with cotton sutures. An incision was then made with a scalpel through the pleura at the line of the demarcation between the emphysematous and normal lung tissue. The emphysematous segment then easily came away from the normal lung tissue with finger-tip dissection. Re-expansion of the remaining portion of the upper lobe revealed that only the subapical segment of the lobe had been removed.

Pathology: Gross Examination.—The gross specimen consisted of a portion of lung tissue weighing 50 gm. It was light and feathery to feel. Crepitation was absent except for the very periphery. The surface was pinkish-white, smooth and glistening. Emphysematous bullae were present beneath the pleural surface.

Microscopic Findings.—Examination of sections of the lung revealed a marked distension of alveoli; many of the alveoli were ruptured and in some areas they appeared to be forming large bullous-like structures. The walls of the alveoli appeared to be of normal or slightly increased thickness. Blood vessels were not prominent within the walls of the alveoli. The larger venules, however, were prominent and filled with red cells.

Diagnosis: Emphysema, hypertrophic type.

The child made an easy postoperative recovery and subsequent RGs (Fig. 1 D) of the chest showed normal-appearing lung completely filling the left hemithorax. Because of the severe pectus excavatum (Fig. 1 E), the heart was unable to shift out of the right chest toward the left. The child was seen in the office and found to be very well 1½ yr. after thoracotomy. Correction of the deformity of the chest was advised, but this advice was not accepted since the parents felt that the child was not embarrased in any way by the deformity.

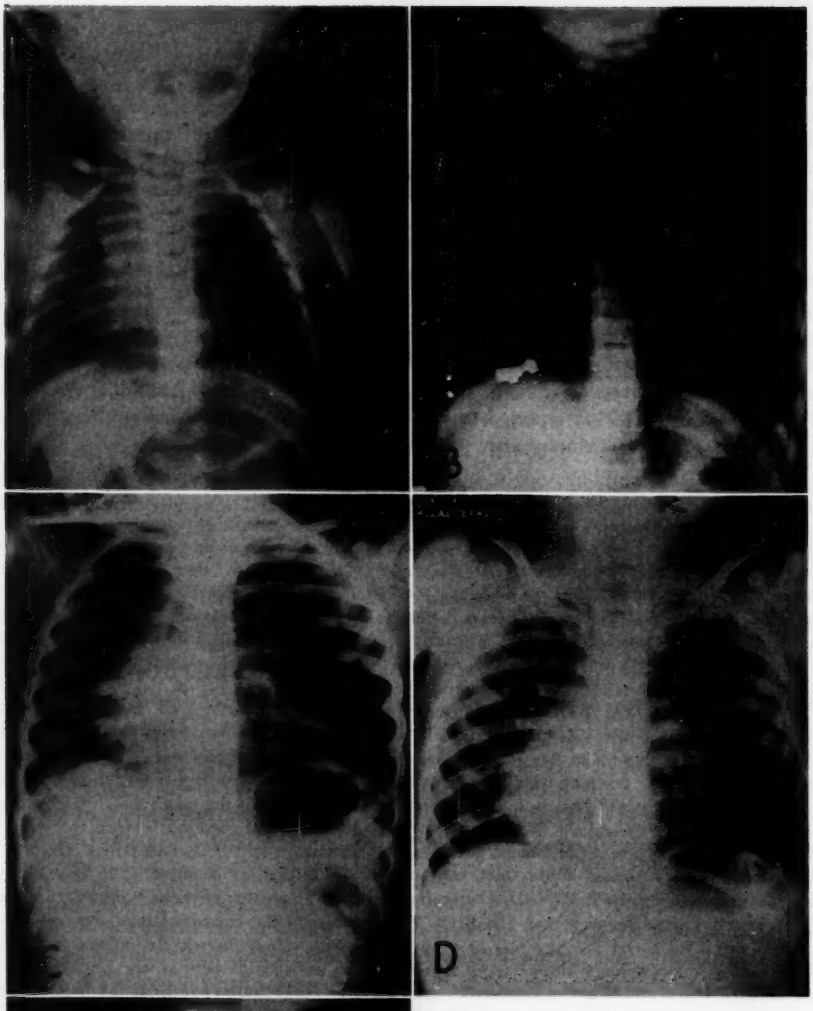


FIG. 1A. Case 1. RG 2 wk. following birth. Note wide upper mediastinal shadow, shift of heart to right, and area of translucency in upper left lung field.

FIG. 1B. Case 1. Child now 2 yr. old. Upper mediastinum normal but heart is still shifted to right and area of translucency in upper left lung field persists.

FIG. 1C. Case 1. Two years later chest RG shows no change.

FIG. 1D. Case 1. Emphysematous segment in left upper lobe has been removed. Left lung appears normal. Heart is still in right chest due to pectus excavatum.

FIG. 1E. Case 1. Lateral view of chest showing severe depression of lower portion of sternum (pectus excavatum).

Case 2: A 7 wk. old white female was admitted to The Children's Medical Center. The child had had a normal delivery and in the neonatal period there had been no history of episodes of aspiration, strangulation, cyanosis or fever. At approximately 2 wk. of age the infant developed a wheeze. She was seen by a physician who made a chest RG. As the result of this examination, a diagnosis of atelectasis of the left upper lobe was made. She was referred to the Children's Medical Center for care. The mother stated that during the preceding 5 wk. the child had had intermittent episodes of rapid breathing with subcostal retraction.

Physical examination revealed a well developed, well nourished white female infant. The child's respirations were more rapid than normal, and there was slight in-pulling of the chondral arch on inspiration. Auscultation over the chest revealed absent breath sounds over the entire right chest

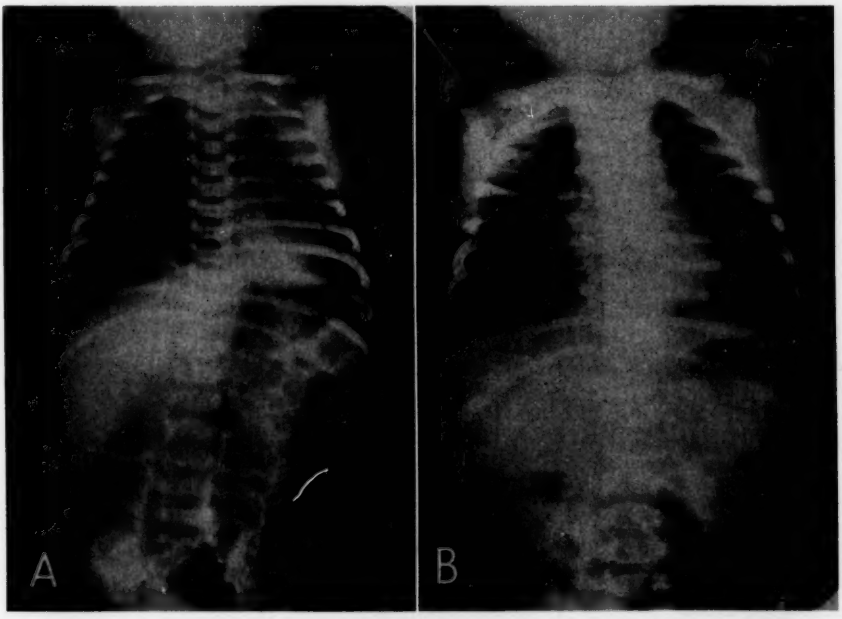


FIG. 2A. Case 2. Emphysematous middle lobe fills entire right hemithorax crowding heart and mediastinal structures into left chest.

FIG. 2B. Case 2. Six weeks following removal of emphysematous right middle lobe chest appears normal.

and the anterior portion of the left chest. The breath sounds over the left chest were somewhat accentuated. The heart sounds were best heard in the left anterior axillary line.

Roentgen Examination: Posterior-anterior (Fig. 2 A) and lateral films of the chest showed a most unusual over-distension of the right lung. In the lateral view, the right lung apparently was passing the anterior mediastinum and pushing the mediastinum and its contents far back. The cardiac silhouette in the lateral view was situated about in the middle of the chest as the result of this displacement posteriorly. In the posteroanterior view the border of the right lung can be seen almost touching the left thoracic wall. As a result, the left upper lobe appears to be atelectatic. The dense shadow seen in the upper portion of the left hemothorax represented a compressed upper lobe not atelectasis due to obstruction.

Conclusions: 1. Unusual over-distension of the right lung due to a ball valve mechanism in the right main bronchus. 2. Herniation of the right lung through the anterior mediastinum. 3. Compression atelectasis of a portion of the left upper lobe and possibly the left lower lobe. 4. Displacement of the mediastinum and its contents to the left and far backward.

Bronchoscopy: Bronchoscopy revealed a left bronchus, the orifice of which was reduced in size because of red swollen mucosa and external pressure. The scope would not enter the left main bronchus, but the sucker tip was introduced into it and a small amount of mucoid material was aspirated. The right bronchi appeared patent but the orifices seemed distorted. Due to the small size of the individual, accurate visualization of the right branch bronchi could not be made.

Since no ball valve obstruction was found, a diagnosis of localized emphysema of a segment of the right lung was made and surgery advised.

Operation (4th hospital day): With the patient under intratracheal anesthesia the right chest was opened through the sixth rib bed. Upon entering the pleura the emphysematous portion of the lung bulged out through the incision completely filling it. Adequate exposure had to be obtained by

FIG. 3. Case 2. Emphysematous right middle lobe which filled entire right hemithorax. Even after removal lobe remained distended.

compressing the emphysematous lung tissue. Further examination revealed that the upper and lower lobes were completely non-air-containing and were compressed into the upper and lower portion of the chest, respectively. The greatly enlarged middle lobe completely filled the right hemithorax and displaced the anterior mediastinum to the left. The emphysematous middle lobe was removed by dissection technic following which the remaining 2 lobes of the right lung expanded well to fill the hemithorax. A small catheter drain was placed in the 8th interspace and connected to a water seal bottle, and the thoracotomy incision closed.

Postoperative Convalescence: Following surgery the child was immediately seen to breathe much better than before operation. The drainage tube was removed on the first postoperative day and the child was allowed to be taken home by her parents on the 5th postoperative day. At this time there was complete disappearance of the wheezing type of respiration and of the in-pulling of the chondral margin on inspiration. RG (Fig. 2b) 6 wk. following surgery showed normal expansion of the right lung and normal position of the mediastinum.

Pathology: Gross Examination (Fig. 3).—The lobe measured 8 x 6 x 3 cm. It was full, pale, pink and hypercrepitant. The pleural surface was smooth and glistening and presented several spreading subserosal blebs. The cut surface was dry, pale and spongy giving a honeycomb appearance. The bronchioles were not conspicuous.

Microscopic Examination.—The air sacs and alveoli generally were distended and empty. The intervening septae were thin, and there was no inflammatory reaction. The blood vessels were small with thin walls. The bronchioles were empty. The bronchial mucosa was normal except for slight chronic inflammatory infiltration. The cause of the emphysema was not evident in the sections. Diagnosis: Emphysema, hypertrophic, right middle lobe.

Etiology

One of the most interesting features of this disease are the possible etiologic factors causing it. Several explanations have been advanced, but none of them seem to fully explain the cause of the condition. Royes[2] described a flap of mucous membrane which occluded 5/8 of the lumen of the bronchus. He postulated that this mucosal flap acted as a valve causing the condition. It is possible to visualize that a freely moving flap of mucosa might occlude a bronchus on inspiration and thus give rise to segmental atelectasis, but it is difficult to understand how a flap of mucosa could cause an expiratory block giving rise to emphysema. No such flap was found in the patients reported here.

The fact that the condition seems to be present at birth or develop shortly following birth causes one to wonder if its occurrence may not be connected in some way with trauma of birth or attempts at resuscitation shortly following birth. Such attempts include vigorous efforts to expand the lung by positive pressure oxygen. Interstitial emphysema of the lung sometimes associated with pneumothorax and interstitial emphysema of the neck and chest has frequently been observed following such trauma immediately following birth. Such emphysema, however, is transient and would not persist for years as in these patients. Also, such a condition would not be localized to a segment or lobe of the lung.

In the patients reported here, there was no history of an upper respiratory infection with excessive mucoid secretion to explain an obstructive type of emphysema. The involved segment or lobe did not seem to be susceptible to infection over a period of time. The segments remained surprisingly stable as to size and in no instance was there associated atelectasis due to mucoid plugging of other bronchi. It does not appear that infection has played a major role in the etiology of this condition.

There seems to be another possible explanation for the occurrence of this type of emphysema. In the examination of the specimens removed, it was observed that the bronchi to these segments were abnormally flaccid. They seemed to be almost devoid of cartilaginous rings as compared with normal bronchi of infants and children at the same stage of development. It is recognized that in some infants there is chondromalacia of the structures of the air passages. The so-called "rose petal epiglottis" is an example of this type. In some infants, the entire tracheobronchial tree is so flaccid that there may be respiratory difficulty especially upon expiration. It seems possible that such a chondromalacia could be localized to the bronchi of a lobe or segment of a lobe so that air would be admitted on inspiration but be trapped by the thin collapsing bronchi on expiration. A segment of lung thus distended could cease to take part in ventilation and would crowd the normal ventilating portions of both lungs.

Diagnosis

Diagnosis of localized hypertrophic emphysema in infants depends upon: (1) history, (2) physical examination, (3) correct interpretation of roentgen films of the chest, (4) bronchoscopic examination and (5) an awareness that there is such a clinical entity. The most important point in the history is the development of a wheeze in the absence of evidence of a respiratory infection. On physical examination there will be noted in-pulling of the chondral arch and lower sternum on inspiration. This is due to obstruction of the air passage caused by compression and distortion of the bronchi to the normal segments by the emphysematous segment. Findings on auscultation will seem to be at variance with the appearance of the chest RG because breath sounds are absent over the pulmonary segments that are most air-containing and accentuated over the apparently atelectatic segments. This seeming paradox is the clue to the diagnosis. Pneumothorax may be suspected upon first glance at the film but the presence of fine linear shadows through the translucent area indicating trabeculae will usually make this differentiation. Bronchoscopy will rule out obstruction of the major bronchi and will reveal only distortion of the lower trachea and major bronchi.

Treatment

Surgical resection of the emphysematous segments or lobe is definitely indicated in this condition. Bronchoscopy is only of diagnostic value. Medical measures such as inhalation of vaporized air and bronchodilators will not improve the ventilation of the involved segments. Resection is easily tolerated by infants having this entity since the near normal is restored, and pulmonary ventilation immediately improved. Resection should be done even though symptoms may not be severe in order to improve the respiratory capacity and to prevent the deformity of the anterior chest wall that is caused by the pull of the diaphragm in the presence of obstruction of the upper air passages. This latter complication occurring in the first case is severe enough to indicate surgical correction.

Summary

Localized hypertrophic emphysema is a distinct clinical entity occurring in infants which seems to be congenital in etiology. The possible explanations of the mechanical factors causing this condition are discussed. Resection of the involved segments or lobe is indicated to improve respiration and prevent the occurrence of pectus excavatum.

References

1. Leahy, L. J., and Butsch, W. L., Surgical management of respiratory emergencies during first few weeks of life, Arch. Surg. **59**:466, 1949.
2. Royes, K., Localized hypertrophic emphysema, Brit. M. J. **2**:659, 1938.
3. Caffey, J., Regional obstructive emphysema in infants and in children, Am. J. Dis. Child. **60**:596, 1940.

Spanish Abstract

Enfisema Hipertrofico Localizado

La ocurrencia de enfisema pulmonar localizado a un segmento de un lóbulo o a un lóbulo total, y el cual no está asociado con aspiracion de cuerpos extraños o con mucosidades tenaces debidas a infecciones de las vías respiratorias superiores, es una condición la cual ha recibido poca atención en la literatura. El diagnóstico de esta condición durante la infancia es muy importante, ya que la resección quirurgica del segmento pulmonar afectado resulta en la mejoria de la respiración del niño y además previene las deformidades del tórax. Usualmente, esta condición aparece durante el primer mes de nacido y se

caracteriza por la presencia de un tipo de respiración sibilante con períodos transitorios de cianosis. A veces se observan retracciones ligeras de las inserciones condrales durante la inspiración. Los signos radiográficos demuestran translucencia a veces afectando todo un hemitórax con desplazamiento del mediastino en dirección contraria del lado afectado. La ausencia de ruidos respiratorios sobre el area que demuestra la mayor translucencia en la placa radiografica es un signo de diagnóstico seguro. La resección quirurgica del segmento afectado es bien tolerada por el niño, y en la mayoria de los casos, la capacidad respiratoria del niño mejora inmediatamente. Se reportan dos casos ilustrativos de esta entidad clinica. Se discuten las causas probables de los factores mecanicos que intervienen en la producción de esta condición.

3810–12 Swiss Avenue

Pediatrics

VOLUME 9 FEBRUARY 1952 NUMBER 2

AMERICAN ACADEMY OF PEDIATRICS, INC. PROCEEDINGS AND REPORTS

THE PRESIDENT'S PAGE

STANDARDS of American medical practice are the highest in the world. Deficiencies presently existing may best be improved by voluntary efforts on the part of the medical profession. One of the obvious problems is the betterment of our public relations. Physicians must spend more time in giving to the public actual facts concerning medical care and in cooperating with lay groups whose activities influence public opinion. The help of every member of the Academy is needed in his home community for intelligent planning and for progress in the solution of this problem.

Our Committee on Public Relations, under the capable chairmanship of Dr. O. L. Stringfield, feels strongly that our efforts must begin with the individual Academy member. The latter can best make his influence felt through active participation in the public relations programs sponsored by the local, county, state and national medical organizations of which he is a member. At a meeting of Dr. Stringfield's Committee in Toronto, on October 23rd, it was decided that the Academy could most effectively contribute to improved public relations by integrating its activities with those of organized medicine as a whole. Television, radio and the press will be utilized as media of expression, in an effort to remove some of the current distrust and misinformation commonly associated with our public contacts. It is suggested that you address any recommendations, criticism or suggestions to a member of this Committee. We, as pediatricians, have an obligation and a responsibility to assume a more active role in our dealings with the public.

The Academy has, by virtue of strengthened liaison with other organizations motivated by similar objectives and ideals, become more influential during recent years in the fields of public health and child welfare. These relationships must be continually developed if we expect to expand the effectiveness of our program.

The Awards Committee, one of the standing committees, is anxious to have a large and representative list of nominees for the Borden and the Mead Johnson honors. For your information, the conditions of each award and the names of all previous recipients are listed below:

1. Borden Award ($1000 and a gold medal).
   a. The award is made for outstanding achievement in research related to infant nutrition.
   b. This research must have been publicly reported.

c. The award is made to one individual or for one project, and the recipient must be a resident of the United States or Canada.

2. Mead Johnson Awards: First, $1000; second, $500.
   a. These are not necessarily granted annually, but only when a piece of work is evaluated as outstanding and worthy of honorarium.
   b. Membership in the Academy is not a requisite; but the grants are limited to residents of the United States and Canada who have finished medical school within the past 15 years.

Award Recipients:

	Borden	First Mead Johnson	Second Mead Johnson
1939		Dr. F. H. Gibbs	Dr. Dorothy Andersen
1940		Dr. Robert E. Gross	Dr. Lee E. Farr
1941		Dr. Rene J. Dubos	Dr. Albert B. Sabin
1942		Dr. David Bodian	Dr. Helen Harrison
		Dr. Howard A. Howe	Dr. H. E. Harrison
1943		Dr. Hattie E. Alexander	Dr. Philip Levine
1944	Dr. Harry H. Gordon Dr. S. Z. Levine	Dr. Fuller Albright	Dr. Josef Warkany
1945	Dr. Edwards A. Park	None	None
1946	Dr. James L. Gamble	Dr. Horace L. Hodes	Dr. Paul Harper
1947	Dr. Grover F. Powers	Dr. Helen Taussig	Dr. Louis K. Diamond
1948	Dr. Dorothy Andersen	Dr. Wolfgang Zuelzer	Dr. Benjamin Spock
1949	Dr. A. H. Washburn	Dr. Nathan Talbot	Dr. Henry Barnett
1950	Dr. Joseph Warkany	Dr. Charles May	Dr. Gertrude Henle
		Dr. Harry Shwachman	Dr. Werner Henle
1951	Dr. Daniel Darrow	Dr. William Wallace	Dr. Victor Najjar

One of the highlights of the scientific program at the annual meeting is the announcement of the Borden and the Mead Johnson awards. For the first time, at the Toronto meeting in October, the official program included both the names of the recipients and the title of their various scientific papers. Progress in our profession is necessarily identified with research. And, each of us will profit by stimulation of original thought and initiative. Maybe you know about some brilliant piece of research which has been overlooked by our Awards Committee. Members of the Committee will be delighted to hear from you. And, it is essential that nominations be sent to Dr. Ralph V. Platou, Chairman, before March 1st, 1952, in order that the Committee may deliberate within ample time for the recipients to present suitable papers at the Chicago meeting next fall.

WARREN W. QUILLIAN, M.D., *President*

SUMMARY REPORT
REGIONAL PEDIATRIC CONFERENCES
1950-51

Sponsored by

THE AMERICAN ACADEMY OF PEDIATRICS

Submitted by

THE COMMITTEE ON MEDICAL EDUCATION

MEMBERS

WARREN R. SISSON, Boston ..... Region I
JAMES L. WILSON, Ann Arbor, Mich. ..... Region II
JOHN MCK. MITCHELL, Philadelphia ..... Region III
ROBERT B. LAWSON, Winston-Salem, N.C. ..... Region IV
RALPH V. PLATOU, New Orleans ..... Region V
JAMES G. HUGHES, Memphis ..... Region VI
HENRY G. PONCHER, Chicago ..... Region VII
LEE FORREST HILL, Des Moines, Iowa, Chairman ..... Region VIII
H. E. THELANDER, San Francisco ..... Region IX
J. HARRY EBBS, Toronto ..... Region X

During 1950-51 10 regional pediatric conferences were held under the sponsorship of the American Academy of Pediatrics. There were from 6 to 10 medical schools in each region, with the exception of Region X which included all of the Canadian medical schools. A member of the Committee on Medical Education served as the "Captain" for his region. Participants were the heads of the pediatrics departments or their representatives from the medical schools in the region, state chairman in the region, district chairmen, and other guests invited at the discretion of the "Captain." A summary report of each regional conference has been prepared and a copy together with a "Summary" of the "summaries" will be sent to all who were invited to attend the conferences, but will not be published elsewhere. A limited number of extra copies will be available. Anyone wishing a copy of the complete report may obtain it by writing the Executive Secretary, Dr. E. H. Christopherson.

Purposely, no common agenda was supplied in the belief that the problems in the regions would differ widely and that there would be value in a later comparison of the approach made to those problems in the different conferences. While main emphasis naturally centered about teaching of pediatrics at the undergraduate, intern and resident level, most conferences extended the scope of their discussions to include state-wide problems of pediatric education of more specific interest to state chairmen. In general the attendance of state chairmen was disappointing.

It is the Committee's hope that improvement in this respect will occur in subsequent years, for it is felt that greatest progress can be made when teachers and practitioners "pool" their interests around the conference table.

The following are a few basic topics selected for comment which came up for discussion in a majority of the conferences.

1. Evaluation or Score Sheet. (This consists of 28 separate items, each of which contributes to the organization and effectiveness of a pediatric department. Each item is assigned a numerical grade ranging from a top figure to zero.) It was used by Dr. John McK. Mitchell in the original survey of pediatric departments. There was general agreement that while it had been most useful for that purpose, it was not practical to continue its use in this way on a yearly basis. Score sheets should be provided at each of the conferences for the convenience of department heads who might wish to

evaluate their own departments. It was suggested that the Committee on Medical Education should stand ready to send a team to any pediatric department requesting a re-evaluation. Also the Committee on Medical Education should be responsible for revising the evaluation schedule according to suggestions coming from the individual conferences.

2. Standardization of Pediatric Departments. In the original survey, wide variation was found among pediatric curricula in such items as a total hours allotted to pediatrics; instructors per student; in- and outpatients per student; number of full-time staff; total beds, including newborn and premature, under pediatric control; total beds per student; budget per student, etc. In none of the conferences was there a formal recommendation for the establishment of minimum or optimum standards which should be met by all pediatric departments. On the contrary, one conference reported that "Pediatric curricula should not be standardized, but the American Academy might well lay down a broad outline of acceptable content considering the course to total 300-350 hours." Another conference stated that the Committee on Medical Education should attempt to establish a recommendation of number of hours which a medical school optimally should devote to the teaching of pediatrics, and an optimum number of pediatric patients for which a medical student should be responsible during his clinical pediatric experience. A figure suggested for ward service was one new patient every two days. From a study of the reports one reaches the conclusion that no one advocates strict standardization but, because of the wide divergencies, some consideration might well be given to what should constitute optimum practices.

3. Didactic vs. Bed-side or Patient Teaching. Nearly every conference had something to say on this topic. The trend away from the didactic lecture and toward teaching around the patient marks one, if not the most definite change in pediatric pedagogy in recent years. In some schools the didactic lecture has been almost completely abandoned, in others, the hours have been greatly curtailed. Those favoring retention of the lecture hours maintain that there is no other way of covering the material. Others say that this cannot be done anyway, so why worry about it. There seems to be little disagreement with the thesis that teaching which arises from the observation of and responsibility for a specific patient is undoubtedly the most valuable type of teaching. Some felt that a minimum number of lecture hours, illustrated if feasible by audio-visual aids, should be utilized to present material which the student might have difficulty finding or understanding in textbooks.

4. Integration of Pediatric Teaching and Other Departments in the Medical School. As stated in one of the reports, teaching at the undergraduate level is designed to train medical students to be doctors, not specialists. In order to do so, interdepartmental barriers should be broken down and replaced by cooperation in planning the program. Basic sciences have many tie-ins with clinical pediatrics, where correlated teaching would be most helpful to the student. This is also true in other major departments such as psychiatry, surgery, orthopedics and the head specialities. Here again the trend is encouragingly away from isolated departmental teaching, and toward horizontal and vertical integration with all departments. The success of this movement would appear to depend much on the personality make-up of the long established department personnel. Outpatient teaching should be emphasized since it simulates actual practice more closely than does inpatient. Inpatient teaching is not to be de-emphasized, but rather outpatient teaching should be stepped-up because of the opportunity it gives to acquaint the student with the "family unit."

5. Growth and Development, Public Health, Well-child Care. The impression is gained from studying the conference reports that educators consider all these subjects of major importance in the training of a doctor whether or not he later becomes a pediatric specialist. However, provision for their integration into the teaching is not as complete in some schools as deemed desirable. The changing emphasis in pediatric practice from physical illness to prevention brings these phases of education into the foreground.

6. Newborn and Premature. Almost all the conferences had something to say about the importance of these disciplines in the teaching of pediatrics at the undergraduate and graduate levels. Apparently, many departments need to improve teaching in these fields. In the conference of Region I, Dr. Stewart Clifford described in detail the teaching of these subjects in current use at the Harvard Medical School. An outline of his remarks is appended to the complete report.

7. Audio-visual Aids. This topic was touched upon in several of the conferences. It seemed to be generally agreed that the Academy through its Committee on Medical Education might well serve as a control clearing station where well prepared teaching films and perhaps teaching Koda-slides could be made available.

8. Preceptorships and Decentralized Programs. "Farming-out" of third or fourth year medical students to general practitioners for brief periods is being tried out in a number of medical schools. Hours are deducted from or added to the total curriculum—not pediatrics. Comments were favorable.

The success of decentralized or affiliation programs with outlying hospitals seemed to depend upon the closeness of the association with the parent hospital, and with the quality of teaching maintained at the affiliate hospital.

9. "Adoption" of Families by Medical Students. In the past too much emphasis in teaching has been placed upon a disease or an organ and too little upon an appreciation of the total impact upon a family which illness or other vicissitudes may have. The principle of assigning a specific family to a freshman medical student whose fortunes, good or bad, he will follow throughout his medical course was reported upon favorably.

10. Intern and Resident Training and Graduate Teaching in Pediatrics. The minimum period spent by an intern on the pediatric service should be 2 months. If he is not intending to go into pediatrics, effort should be made to plan especially for his training. Several conferences made the point that pediatric services approved for residency training should have frequent re-evaluations. Graduate courses for equivalent amount of time spent are inferior to good residents.

11. Research. The basic function of a department of pediatrics lies in the area of (1) Clinical Teaching, (2) Research and (3) Service. A pediatric department should be so organized that none overshadows the others and all 3 are developed to their optimum potential. The first 2 years of the pediatric resident's specialized training should be along the broad principles of fundamental pediatrics and should not be diluted by excessive time spent on isolated research.

12. Responsibility of Medical Schools for Postgraduate Teaching. There was full agreement that medical schools had such a responsibility. Chief effort should be directed toward the education of the general practitioner in pediatrics. Pediatricians have access to their national, state and local societies which meets their needs satisfactorily. At least 20% of state medical meeting programs should be on pediatric subjects. Short 1 or 2 day courses at the school, or in the field at the county level, appear to be most successful when a registration fee is charged. Cooperation with the state medical society and the Health Department is essential.

13. Budgets. Lack of adequate finances is a handicap to the improvement of pediatric teaching in many medical schools. Additional funds which are unrestricted are badly needed. When too large a proportion of department budgets is derived from sources other than the medical schools, such as grants, sound planning for the future is made difficult because of the risk that the monies from these sources may be cut off at any time.

In none of the conferences was there an expression of opinion as to whether financial aid for medical education should stem from federal, state, or private sources.

PHYSIOLOGICAL CONSIDERATION OF RESPIRATORY DISEASE

A Symposium

JULIUS H. COMROE, M.D., *Chairman*
Graduate School of Medicine, University of Pennsylvania, Philadelphia

RESPIRATORY AND PULMONARY PHYSIOLOGY
JULIUS H. COMROE, M.D.

NOTES ON PHYSIOLOGICAL BASIS IN CLINICAL PEDIATRICS SITUATIONS WHICH ALTER PULMONARY VENTILATION
JAMES L. WILSON, M.D.
University Hospital, Ann Arbor, Mich.

CYSTIC DISEASE AND EMPHYSEMA OF LUNGS, CONGENITAL AND ACQUIRED
WILLIS J. POTTS, M.D.
Childrens' Memorial Hospital, Chicago

POLIOMYELITIS AS IT AFFECTS RESPIRATION
JAMES L. WHITTENBERGER, M.D.
Harvard School of Public Health, Boston

Presented at the Annual Meeting of the American Academy of Pediatrics, Toronto, Oct. 22, 1951

RESPIRATORY AND PULMONARY PHYSIOLOGY

JULIUS H. COMROE, M.D.

A. Physiologic Factors Concerned in the Regulation of Respiration

Physiologists now agree that there is a medullary respiratory center which has intrinsic rhythmicity. Nevertheless this center can be influenced profoundly by many chemical and nervous factors. One of the most important of these is carbon dioxide. Under ordinary conditions the medullary center is exquisitely sensitive to changes in carbon dioxide pressure. When the respiratory center is depressed (by deep anesthesia, large doses of morphine or barbiturates, trauma, cerebral edema, increased intracranial pressure, severe anoxia or by high concentrations of carbon dioxide itself) it is no longer responsive to carbon dioxide though it may still permit reflex activity and continuation of respiration.

Anoxemia may also stimulate respiration; this occurs through reflexes originating in chemoreceptors of the carotid and aortic bodies. It appears certain that these chemoreceptors are functioning in the normal full-term newborn though they may not be functioning or functioning properly in prematures. When these chemoreceptors are in operation, anoxia will stimulate respiration and oxygen therapy will abolish such hyperpnea. When the chemoreceptors are not in action, one would expect no reflex effects from either oxygen or anoxia; oxygen therapy, however, might relieve cerebral ischemia and permit respiration to improve.

B. Physiologic Methods for Evaluating Respiratory and Pulmonary Function

The function of the lungs is primarily to oxygenate the venous blood and to remove excess carbon dioxide from it. To accomplish this, there must be normal respiratory volumes, normal lung volumes and aerating surface, even distribution of the inspired gas to the alveoli, unimpaired diffusion across the alveolar capillary membrane, and uniform distribution of pulmonary capillary blood flow to the functioning alveoli. Tests were described which permit the measurement of these factors in patients with pulmonary disorders. It is recognized that data obtained from these tests often does not permit the physician to determine why a patient is dyspneic. Newer tests measuring the total work of breathing and the work of the various component parts of breathing should shed new light upon the problem of dyspnea.

NOTES ON PHYSIOLOGICAL BASIS IN CLINICAL PEDIATRICS SITUATIONS WHICH ALTER PULMONARY VENTILATION

JAMES L. WILSON, M.D.

A. Clinical Recognition of Abnormal Respiration

There is no simple or direct way by physiologic laboratory technics to determine alveolar ventilation, which is the measure of efficiency of absorption of oxygen or secretion of CO_2. Alveolar ventilation is a complex resulting from many factors, some of which can be measured, but the sum of all the studies cannot give a direct answer. Studies of CO_2 content and pH with estimation of alveolar pCO_2 are the best laboratory aids at present available. The oxygen saturation hemoglobin is not as reliable a guide for the detection of deficiences of alveolar ventilation.

Observation of a patient by a skilled clinician can go a long way towards evaluating alveolar ventilation. The recognition and evaluation of dyspnea is best accomplished by simple but informed observation. One studies in an orderly fashion and with some attempt at quantitative evaluation (a) rate, (b) rhythm, (c) depth and (d) the shape of the respiratory curve. The last is the hardest to evaluate. The rate, efficiency of the shape, the depth of respiration modified by its regularity or irregularity, results in a more or less efficient pulmonary ventilation.

It is important to estimate the effectiveness of respiratory effort and to realize that an effective respiration resulting in normal alveolar ventilation may be made at the cost of great effort, which eventually may fail. One, therefore, cannot be satisfied only with a physiologic estimation of the results of respiratory effort, but must also evaluate the effort that is being used to produce this respiration.

The technic of peroral auscultation is of great aid in evaluating the depth of respiration as well as any interference by partial respiratory obstruction. Listening with a stethoscope over the nose and mouth of a patient can enable one to get a fairly accurate idea of the "curve" of respiration, and so its efficiency. A simple diagram is used for illustration.

B. Cause of abnormal pulmonary ventilation

I. Primary disturbance of the nervous control of respiration caused by CNS pathology.

a. Meningitis

b. Encephalitis

c. Poisoning

d. Anoxia (particularly in the newborn)

Any of these conditions can cause a primary disturbance of the respiratory center. In the case of meningitis and encephalitis, usually manifested by hyperpnea, though not necessarily, any gross irregularity of breathing may result. The first symptom of meningitis or encephalitis in an infant may be an hyperpnea or a grossly irregular respiration. Anoxia usually does not result in hyperpnea, that is, severe anoxia, but quickly depresses respiratory effort or makes it irregular. The first effect of anoxia, however, may result in hyperventilation. Irregularities of breathing are more common than either a slow depressed respiration or an hyperpnea.

II. Caused by disturbances in acid base equilibrium.

a. Vomiting

b. Diarrhea and dehydration with secondary kidney defect

c. Primary kidney defect

d. Poisoning

We are familiar with hyperpnea as a compensating mechanism to prevent a great change in pH resulting from the accumulation of some foreign acid element in the blood serum, such as in ketosis, which specifically results from starvation or vomiting in infants. As common is the accumulation of chloride and organic acid due to renal dysfunction, itself the result of dehydration from diarrhea. In these circumstances CO_2 is excreted to make room for other but abnormal acid radicals.

Poisoning, such as with ammonium chloride, can result in a direct CNS stimulation of respiration due to a true acidosis.

III. Primary pulmonary pathology

Here we have to consider obstructive lesions in the respiratory tract, asthma, bronchitis, capillary bronchitis, or the reflex disturbance of respiration which we get in a case of lobar pneumonia, where we have rapid shallow respiration, not due to important encroachment on the pulmonary space but due to vagal reflexes. Accumulation of CO_2 may result.

IV. Defects in circulation directly interfering with ventilation.

V. Neuromuscular defects such as congenital defects with hypotonia or amyotonia, or such paralysis as poliomyelitis with respiratory muscle involvement. These lead to direct respiratory failure with CO_2 acidosis as well as anoxia.

CYSTIC DISEASE AND EMPHYSEMA OF LUNGS, CONGENITAL AND ACQUIRED

WILLIS J. POTTS, M.D.

In the otherwise normal infant there are 2 primary reasons for inadequate respiration: obstruction in the air passages and inadequate absorption area. The former is the field of the endoscopist. A few conditions illustrative of the latter will be discussed.

Mediastinal emphysema is caused by too vigorous artificial respiration in the newborn, coughing, choking, asthma, etc. If an alveolus breaks in the lung mediastinal emphysema may follow. If the alveolus breaks through the pleura pneumothorax results and requires emergency treatment.

Lobar emphysema in infants may be due to obstruction in a bronchus or it may develop without demonstrable cause. If no obstruction in the bronchus exists and if the offending emphysematous lobe causes respiratory distress it must be removed.

Congenital cysts of the lung are fairly common in early infancy and produce severe dyspnea and cyanosis. Emergency relief is often necessary. Surgical removal of the offending lobe yields excellent results.

Acquired cysts of the lung in infancy usually occur in connection with staphylococcic pneumonia. The cysts vary greatly in in size and therefore may or may not produce symptoms. The treatment is definitely conservative.

These conditions will be illustrated with lantern slides.

POLIOMYELITIS AS IT AFFECTS RESPIRATION

JAMES L. WHITTENBERGER, M.D.

Although its paralytic effect on the respiratory motor unit is probably the most common respiratory defect due to poliomyelitis, the disease frequently and seriously affects may other aspects of the respiratory system. Disturbances of reflex and secretory activities in the pharynx produce troublesome respiratory complications. Medullary involvement may critically affect both the nervous and chemical aspects of the control centers. Closely related involvement of circulatory centers in the medulla affect respiration indirectly, particularly because of the close interrelationships of pulmonary circulation and lung function. Circulatory along with other possible factors operating in the lungs lead to pulmonary edema and atelectasis. The latter respiratory complications of poliomyelitis interfere seriously with oxygen supply to the body, whereas deficiency of ventilation due to muscle paralysis or other factors leads primarily to carbon dioxide retention and respiratory acidosis.

Measures designed to correct respiratory dysfunction must be considered as to whether they specifically correct a defect and whether they may at the same time introduce harm or hazard. Respiratory obstruction urgently requires correction by postural drainage, aspiration and sometimes tracheotomy; a too-small tracheotomy tube constitutes respiratory obstruction and the airway is sometimes further compromised by insertion of a catheter supplying oxygen. Ventilatory deficiency is primarily a problem in carbon dioxide removal and must be treated by increasing ventilation; oxygen administered without attention to ventilation may make respiratory acidosis worse. Several methods are available for increasing pulmonary ventilation; the body respirator is rightly the most widely used and safest. The physiologic effects of the respirator are the same as those of pressure breathing given by a mask over the face. Combinations of the 2 methods of applying pressure have been used for nursing convenience and for increasing ventilation when pulmonary edema or high airway resistance increase the amount of pressure necessary to produce an adequate tidal volume. The best guide to the adequacy of pulmonary ventilation is measurement of alveolar carbon dioxide or arterial pH and carbon dioxide. If ventilation is satisfactory and hypoxia remains, oxygen should be added to the inspired air. However, hypoxia may be present on a circulatory basis in the presence of an adequate or even excessive ventilation; in this event, the circulatory depression may be due to excessive negative pressure in the tank and may be corrected by addition of a positive expiratory phase, with corresponding decrease of the negativity during inspiration.

Other aids to respiration suitable for special needs are rocking beds, chest respirators, and apparatus for electrically stimulating the phrenic nerve.

Round Table Discussion

PREVENTION OF ACCIDENTS IN CHILDHOOD

GEORGE M. WHEATLEY, M.D., *Chairman,* New York City; JAY M. ARENA, M.D., Durham, N.C.

ROBERT H. KOTTE, M.D., Cincinnati, and BENJAMIN J. HOYER, M.D., Cincinnati, *Secretaries*

Chairman Wheatley: Our theme is a discussion of prevention. We want to discuss the question: How can we help prevent accidents in children? The meeting will be divided into 2 parts. Dr. Arena and I will outline the accident problem for the first part. For the second part, we will discuss the preventive aspects and what pediatricians can do about preventing accidents. We want you to do most of the talking in this part.

I would like to give you a brief picture of the dimensions of the accident problem.

1. It is the leading cause of deaths ages 1-14; kills about 14,000 at these ages annually—more than the next 6 combined (pneumonia, congenital anomalies, cancer, tuberculosis, leukemia, heart disease).
2. Every year between ages 1-5 kills twice as many children as rubeola, scarlet fever, pertussis, diphtheria, dysentery, tuberculosis and poliomyelitis combined.
3. For every fatal accident, it is estimated there are 90-150 severe injuries. No comprehensive studies are available to show the magnitude in terms of injury, cost of treatment, permanent disability in the United States child population. English hospital admission study showed 22% of the accidents requiring hospital treatment happened to children under the age of 5 years, though this age group constituted only 8% of the population.
4. About a third of all fatal accidents to children (1-14) occur in the home; for those under 5 years of age, nearly half the fatal accidents are home accidents. The home is a much more important site than this for injury to children, if we include nonfatal accidents because deaths caused by motor vehicles influences the fatal accident picture.
5. In children 1-14, motor vehicles cause about 35% of all accident deaths. Burns and fires account for 28%.

As one pediatrician has recently expressed it: "With one-third of all children who died dying in accidents, I have come to the conclusion that as long as I work only on the prevention of disease, I am only partly serving my patient's interest."

Why accident control program for children at this time?

There has been virtually no improvement in accident fatality rate in children for the past 10 years.

Prior to the war, the trend was downward at a promising rate which hit the low point for all ages in 1940. The rate then began rising with the sharpest increase in the very young children, aged 1 to 4 years. It is believed that important factors were family dislocations and mothers working which resulted in lessened supervision of young children. Also the record birth rates during these years resulted in a high number of young children exposed to the risk of accidents. These killed and maimed children are the forgotten casualties of World War II.

Since we appear to be entering another era of great mobilization of man and woman power for industrial production and possibly higher birth rates, it is timely to recognize that these unusual conditions represent an increased accident hazard to children. We must plan now how to prevent the waste of young lives which occurred in the past 10 years.

The attack on the problem is a three-pronged one involving Education, Engineering and Enforcement, with the main effort on education. This involves education of the profession as well as the public. We find that most pediatricians are interested in accident prevention and incorporate it in health supervision. Many other physicians who see young children are not aware of the importance of

Presented at the Annual Meeting of the American Academy of Pediatrics, Toronto, Oct. 22, 1951.

advising parents about how they may prevent accidents. We want to encourage discussion of accident prevention at medical society meetings, by discussion of accident case histories in hospital history meetings and conferences, and by surveys and other technics which will arouse interest in the study of the frequency and the cause of accidents. The education of the public and of the channels of communication such as newspapers, radio, TV and group meetings, should be used. The most effective, however, is the person-to-person guidance which the physician can give in health supervision. Some physicians are giving safety check lists to parents and also booklets to read.

Engineering is being approached through the study of clothing, toys and other equipment for children which may be associated or involved in an accident to them. In a recent questionnaire sent, as you know, to members of the Academy to find out the frequency with which flammable clothing was associated with burns, poisonings occurred in practice, and strangulation or suffocation was due to faulty construction of harnesses and cribs, we received reports on 2,781 cases. Of these, half were due to poisonings; burns accounted for about one-third, of which flammable clothing was the contributing factor in about half of these cases, including 40 fatalities. There were 136 cases of strangulation or suffocation; 255 nonfatal and 23 fatal cases due to poisoning from toxic substances in paint; 357 nonfatal and 20 fatal cases due to accidental ingestion of medicine; 696 nonfatal and 19 fatal cases due to ingestion of disinfectants and other common household substances.

The most striking information from this survey of pediatric practice is the frequency with which poisoning occurs. I would like to ask Dr. Arena to discuss this.

Dr. Arena: Poisons contained in household agents are responsible for most of these unfortunate deaths due to accidental poisoning. If all drugs and household agents that contain poison were made inaccessible to children, such poisonings could be almost entirely prevented. The number of children who have been accidentally poisoned as a result of parental carelessness is truly tragic.

Since most infants and children are poisoned in or near the home of these agents, at least 2 preventive measures should be attempted. First: parents should be informed and educated to the dangers that lie ahead for their infant. As Dietrich so aptly puts it, they must be shown that pimples and pounds are relatively unimportant problems. Accidents present a greater hazard than the threats our too thoroughly propagandized society ordinarily fears for its children. This can be accomplished in part by offering an accident handbook at the first year check-up with a list of various household agents containing poisons. Another measure would be more stringent Federal or State laws. This is the third point in the three-pronged program of Education, Engineering and Enforcement, earlier mentioned by Dr. Wheatley.

The Federal Caustic Poison Act enforced by the Food and Drug Administration requires that the word "Poison" and an acceptable antidote be placed prominently on the label of a household package of a preparation which contains more than a specified amount of any one of the following ingredients: hydrochloric acid, sulfuric acid, nitric acid, carbolic acid, oxalic acid, any salt of oxalic acid, acetic acid, hypochlorous acid, potassium hydroxide, sodium hydroxide, silver nitrate and ammonia.

The Federal Food, Drug, and Cosmetic Act, also enforced by the Food and Drug Administration, does not require the use of the poison legend on any drug preparation.

The Federal Insecticide, Fungicide and Rodenticide Act of 1947, enforced by the Department of Agriculture, requires that certain white economic poisons be colored and requires that the labels of economic poisons toxic to man bear the skull and crossbones and the word "poison" prominently in red on a background of contrasting color with a statement of the antidote for the economic poison.

Chairman Wheatley: A study of poisoning in children under 5 years of age admitted to the New Jersey Medical Center showed kerosene to be the most common cause of poisoning. The hospital is near a veterans' project where kerosene is used for household cooking and heating.

Dr. Arena: In our section, kerosene is the most common cause of poisoning. I thought we were the only ones to combat the kerosene poisoning problem.

Dr. J. K. Mack, Springfield, Ill.: We have kerosene poisoning in our section.

Dr. Edith M. Meyers, Oakland, Calif.: Because of the large number of ants in California, the various ant powders and pastes are our chief problem.

Dr. Arena: Lye is the most acute poisoning in North Carolina. A study of lye poisoning has been made in the large hospitals in our State. A social worker estimated that one case of lye poisoning cost the State of North Carolina $8,000. Most of these cases are among the indigent. No doubt other sections have their particular problems.

Dr. Hoyer: I would like to bring up a problem I ran into. It is a question of nomenclature. I

am interested in lead poisoning and had the need to request from the local health department the number of deaths from lead poisoning. The number reported to me was not as great as the number I knew existed. In investigating further, I found that the deaths from lead poisoning had been classified as encephalopathy.

Dr. Kotte: The Children's and Cincinnati General Hospitals, the Cincinnati Board of Health and the Kettering Laboratory are cooperating in a study of lead poisoning in children.

Question: How does a child get lead poisoning?

Dr. Kotte: Usually from chewing on painted surfaces such as window sills and repainted furniture, or from eating painted plaster. One must advise parents not to use paints for inside painting that contain more than 2% lead.

Dr. Montgomery Blair, Washington, D.C.: We have had 11 deaths from lead poisoning recently. There have been 6 deaths from potassium bromate poisoning from home permanent wave products.

Dr. Arena: Toni stopped using the bromates.

Chairman Wheatley: In getting back to Dr. Hoyer's point about nomenclature, we need more accurate diagnosis for proper classification. To study poisonings satisfactorily, a toxicologic laboratory should be available to all physicians. Even in a city as large as New York, I find that the only place a physician can get toxicologic services is in the Coroner's office.

Dr. Hoyer: How about deaths from aspirin poisoning? Are they classified under aspirin poisoning, or alkalosis or acidosis? The Academy could make such a study.

Chairman Wheatley: Chronic poisoning, due to lead, must also be thought of as well as the acute poisonings.

Dr. Arena: There are 1,000 deaths from poisonings each year. No doubt many are missed. I would like to tell about an experience we had recently. A little child of 4 years died as the result of ingesting camphorated oil. The mother had used the oil as a remedy for a respiratory infection. The child got hold of the bottle and drank some. The mother realized what had happened. She read the label. There was nothing on the label to indicate that it was poisonous. She was an intelligent individual and reasoned that if it were poisonous, surely there would be a law requiring a poison label, or something to indicate an antidote, or a warning. So she did nothing. About 3 hours later symptoms developed. The child was brought to our hospital. In spite of heroic measures, the child died. She was the only child. The mother kept repeating "If I only had known." I investigated the Federal laws. There are 3 laws governing the sale of poisons: The Federal Caustic Poisons Act, the Federal Food, Drug and Cosmetics Act under the Federal Food and Drug Administration, and the Federal Insecticide and Fungus Act under the Department of Agriculture.

These Federal Acts are fine and useful as far as they go. However, they are far from adequate. When inquiring about more comprehensive Federal laws, the following reply was received from Dr. Erwin E. Nelson, Medical Director of the Federal Security Agency.

"We are aware of the needless tragedies caused by accidental poisonings in cases where the poisonous article is not packaged or labeled in such a manner as to call attention to its poisonous properties. When a bill was introduced into the Senate in 1949 (S. 2193, 81st Congress) to require distinctive containers for certain poisonous drugs, we expressed our support of the purpose of the bill. We suggested that the Federal Caustic Poison Act should be broadened to cover other poisonous substances than those now specified in it, including drugs, and that the Federal Security Administrator be empowered, after opportunity for hearing, to add poisonous substances to the list; that provision be made for distinctive safety containers, distinctive coloring of the article were required, and, in the case of poisonous liquids which might intrigue children, bottles with openings sufficiently constricted to make it unlikely that a child would ingest a lethal quantity.

"S. 2193 was not passed by the 81st Congress and, so far as we know, no similar bill has been introduced into the 82nd Congress."

The medical profession should see to it that their elected representatives in Congress are made aware of the importance of more stringent Federal laws concerning the packaging and labeling of poisonous articles or agents.

Dr. Hoyer: Can the Academy get word to Washington on the bill?

Dr. Arena: Let's work on something better.

Dr. James H. Wallace, Oak Park, Ill.: Legislation should be more at the local level.

Chairman Wheatley: The answer is yes on both levels. For intelligent action we need more information about each poisoning and more study on type of law to be recommended.

Dr. Wix, Sewickley, Pa.: In the case of aspirin, what would you put on the label? What dose would be put on? I believe the problem is one of educating the parents.

Chairman Wheatley: Most of the cases of poisoning occur in the 1 to 4 year old group. This group cannot read labels.

Dr. Arena: There are 2 methods of approaching the problem. One is through education of the parents, informing them of the dangers; and the other is in more stringent local, state and federal laws.

Dr. George F. Patterson, Cincinnati: I believe the bulletin board in the office is a visual means of education.

Dr. Arena: I have a bulletin board in my office which is used for other subjects as well as for poisons and accidents.

Dr. Mack: The question is what is the most practical way of teaching the parents?

Chairman Wheatley: Here are some ways of bringing the subject before the people. Dr. Bost sent to me these pamphlets which the Franklin Hospital of San Francisco developed. He has a leaflet for his private patients also. The Minnesota Department of Health has a pamphlet called "Protect Toddlers from Accidents." The Georgia Department of Public Health puts advice on accident prevention on the reverse side of the diet instruction cards which mothers receive in the well child conference.

Dr. A. T. Martin, New York City: What is the National Safety Council doing?

Chairman Wheatley: The Academy and the National Safety Council have been cooperating. I have been appointed to represent the Academy on the Council Board. The Home Safety Conference of the Council has developed pamphlets on Christmas safety and baby sitters which can be had for distribution.

Dr. Hoyer: One method is for the doctors to get together and discuss their experiences and from that information, formulate a report that can be given to physicians and parents.

Dr. Gerald M. Cline, Bloomington, Ill.: Have the PTA's been consulted?

Chairman Wheatley: Yes, we have offered our services, but we have no response as yet. In California, the Prudential Life Insurance Company has underwritten a very intense and successful community safety program to prevent accidents to children. This has been done in cooperation with local safety councils, medical schools and hospitals. Dr. Esther Clark and Dr. Harry Dietrich, members of our Committee, have taken an active part in this statewide campaign. There is a motion picture on child safety for school children produced by Sid Davis Productions, Los Angeles, which Dr. Dietrich helped to develop.

Dr. Cline: The Academy's Committee on Camps is putting out a booklet and a film. Accident prevention is included in both.

Dr. Neil C. Stone, Poughkeepsie, N.Y.: I prefer slides such as Dr. Wheatley used to film.

Dr. Wallace: A fertile field for educating the public is to direct attention of the public health nurse to the accident prevention problem.

Dr. Park J. White, St. Louis: Dr. Wheatley, does your Committee feel that the Academy should prepare a booklet to be purchased and circulated by medical societies and health departments? Also, let me call your attention to a recent study we have made in St. Louis which indicates that Negro and white children have about the same accident rates, although kerosene poisoning, scalds and flame burns are definitely more frequent among the Negro children.

Chairman Wheatley: The Committee is preparing a booklet called "Are You Using the New Safety Vaccine?" This will be made available to pediatricians and other physicians who do health supervision. The booklet will relate safety education to the stages of growth and development in children from infancy up to 5 years. We hope the booklet will impress the practicing physician with his opportunity for safety education and encourage incorporation of safety education into health supervision as a new kind of immunization—an immunization of the parent rather than the child.

Dr. Arena: A large marble-sized vitamin pill as demonstrated at the booth is a potential source of choking. I told the salesman so. Someone else had just told him the same thing. He did not like our remarks.

Chairman Wheatley: One of the most serious accidents is due to burns. In the reports received from the members of the Academy, burns represented 30% of all reported cases. More than half of these were said to be associated with clothing which caught fire. Some of you may recall the tragic accidents that were reported from an extremely flammable type of clothing used on cowboy suits

several years ago. This suit was quickly taken off the market, but there are other types of highly flammable textiles that find their way into clothing for children. Our Committee is interested in standards that have been developed to test the flammability of clothing. We believe that some accidents could be prevented if parents knew what clothing is flame-resistant or less flammable. This is an example of the engineering approach to accident prevention. Another example is the manufacture of harnesses and restraints which are used on children. In the reports from members of the Academy to our Committee, strangulation by harnesses or straps accounted for 18 fatalities and 34 nonfatal accidents.

One pediatrician groups 7 nonfatal and 1 fatal case together as the circumstances were similar, making a compositive picture more informative. All were sleeping in a bag tied down to the 4 corners of the crib. The bag had a zipper down the front ending in a neckband through which the baby's head protruded. All were at the toddling age (10 to 16 months). Apparently they all did the same thing—turned on one side and "walked up" the rungs of the crib, thereby rotating their bodies in the bed by means of the leverage of pushing a foot on one rung after another. When they got a little beyond a cross-wise position, the neckband twisted tight around the neck, apparently quite suddenly, so that they were garroted. The reason the doctor thought the twist was sudden was that only one was heard to cry out, and he gave only a few squeaks. The others were discovered because their thrashing about in the bed was heard. They all had scleral and facial petechiae for several weeks and 3 of them were aphonic for about a week.

Earlier, lead poisoning was referred to. We are including this problem in our investigation of the prevention of accidents through engineering. It may be possible to develop standards for the labeling of paint so that it might indicate that a paint is safe to use on objects with which a small child may come in contact.

These problems are going to be discussed at a meeting requested by our Academy Committee and sponsored by the American Standards Association on December 5, 1951. Representatives from national, medical, public health, parent, governmental and trade associations are invited to this meeting to determine if projects can be set up to create standards which might reduce the hazard to children of certain manufactured articles.

Dr. Robinson, Hamilton, Ohio: I know of a baby who, while in a harness, vomited straight up and almost strangled. The problem was getting the child loose quick enough to prevent aspiration.

Dr. Katherine D. Brownell, New York City: In our hospital we use a fish net. We have had no bad experiences.

Question: What do you mean by a fish net?

Dr Arena: It is a thin net that fits over the crib. It allows the baby to stand but not to fall out.

Dr. Ferris, Chicopee, Mass.: That does not solve the problem of keeping the baby warm.

Dr. King G. Woodward, Rockford, Ill.: Has anyone ever heard of a child frozen to death in his crib? I have not. I believe the fear of a child getting a cold from lack of covering is overemphasized.

Comment: I have used the same system with success.

Dr. Kotte, Cincinnati: A bulletin given us stated that the Gift Fair at the Hospital for Sick Children in Toronto has a harness for sale. Has anyone here seen it?

Dr. Bernard I. Michaels, Pittsburgh: I have. One side was loose, the child was held up by the crotch. I believe one could strangle.

Dr. Kotte, Cincinnati: The day on which I left for the Chicago meeting last year one of my patients was strangled in a blanket type that tied to the sides.

Chairman Wheatley: I believe some of the suffocation deaths may occur when a baby is at that stage of development when he can turn partly over but hasn't full control to turn freely from his back onto his face and to his back again.

Dr. Hoyer: One must not forget that there can be dangers from the bumper guard.

Dr. H. H. Shuman, Springfield, Mass.: When babies slept on the floor, there were no such accidents. The mattress must be firm. All creases must be eliminated. Babies should not sleep with parents.

Dr. Hoyer: The mattress must fit the bed.

Dr. H. B. Mark, Riverton, N.J.: Is it true that not all deaths are due to suffocation?

Chairman Wheatley: Yes. Probably most are not due to suffocation. There is good evidence that many are due to acute infections which are unrecognized. It is a subject for further investigation. The

Children's Bureau is aiding a study under the direction of Dr. Sidney Farber of Boston to clarify this situation. Research on accidents is greatly needed. A pilot study of Babies Hospital, Presbyterian Medical Center, financed by the Metropolitan Life Insurance Company is being undertaken to determine how to investigate the accident prone child. The project is under the direction of Dr. William Langford.

Dr. E. O. Jodar, Detroit: My pet peeve is accidents from wringers on washing machines. I have had 76 such cases, 2 of which were serious. I wrote to 2 companies; one company did not answer my letter, the other said it would investigate the subject.

Chairman Wheatley: We must not put too much faith in legislation or engineering to control accidents. Education of parents and children is more important. For example, it is doubtful if we can make a cook stove "foolproof" so as not to be dangerous for a child. A stove is essential in the home. The child must be taught how to live safely in the kitchen.

Dr. Kotte: It is my first duty to acknowledge the indebtedness and to express the gratitude of the Cincinnati Pediatric Society to Dr. Wheatley and his associates in the Metropolitan Life Insurance Company. We have called on Dr. Wheatley for advice and for material help in the form of literature. He has always responded. In trying to develop a program of accident prevention for the children of Cincinnati, we found that the support of other organizations both medical and lay were needed. When a full time Executive Director was appointed for the Greater Cincinnati Safety Council, there was a marked increase in accomplishment in all forms of childhood safety.

Dr. Martin: Was he a paid executive?

Dr. Kotte: Yes.

Chairman Wheatley: In summary, I hope our discussion has made it clear that accident prevention is an important part of pediatric practice. We have discussed the magnitude of the problem, emphasizing the frequency of poisonings. We have discussed ways of educating families to avoid accidents. We have also suggested some of the opportunities for professional education and participation in community safety activities. There are, of course, many gaps in our knowledge and important areas for further study and emphasis. Some of these are: (1) the need for better diagnostic work-up of many of these, particularly poisonings. Here physicians will be helped if they have toxicologic laboratory facilities in their communities; (2) there needs to be an evaluation of the educational methods used for parent-and-patient education; (3) there should be more thorough investigation of the circumstances leading up to accidents. The whole area of child behavior and emotional health is involved here.

To be effective, accident prevention has to be incorporated into everyday living.

Pediatrics

VOLUME 9 FEBRUARY 1952 NUMBER 2

SPECIAL SECTIONS

THE PEDIATRICIAN AND THE PUBLIC

"A forum where discussion could be free, intelligent and continuous."

PAUL A. HARPER, M.D., *Editor*

Statements appearing in this column do not necessarily reflect the opinion of the editor nor are they to be interpreted as the official opinion of the Academy.

COMMUNICATION FROM PHILLIP E. ROTHMAN, M.D.

DEAR DR. HARPER:

I am submitting the enclosed manuscript for publication in PEDIATRICS in "The Pediatrician and the Public."

PHILLIP E. ROTHMAN, M.D.

THE QUALITY OF MEDICAL CARE

PHILLIP E. ROTHMAN, M.D.
Los Angeles

THESE are days of brilliant achievements in medical science. Research progresses with incredible rapidity. Each advance creates additional problems; former gains are often neglected. The attention of the medical profession is occupied with so many issues of immediate importance that the problems affecting the quality of medical care have been pushed aside. In an attempt to appraise the present difficulties, it is helpful to recall past experiences.

Thirty-three years after Roentgen's announcement of "a new kind of ray," Thayer[1] issued the following warning: "It is a sad commentary on human weakness, the manner in which the discovery of a new method of investigation of great help, such as roentgenology, has led the medical public to neglect those fundamental methods of study which are far more important in themselves. . . . The information supplied by an X-ray plate is often of immense complementary value. Alone and without the information afforded by the history, the appearance of the patient and the results of physical examination, it is often of no more value than that afforded by percussion alone—indeed less. For he who percusses the chest cannot fail to observe the patient."

In a similar manner, the course of events that followed the development of electrocardiography has been described by Levine:[2] "During the same period of brilliant advances, older and simpler methods of examination have suffered. This is not surprising or incomprehensible. The interest and energy expended in the development of the new have taken place at the expense and sacrifice in the application of the old. The greater the time spent in taking three electrocardiographic leads and later nine and now twelve leads, the less time is left to elicit an adequate history of the case or to auscult the heart properly. The teaching curriculum in the medical schools has become so overwhelmed with new fields of medical and correlated knowledge, that some of the old teaching and emphasis has had to be curtailed. As a result of this change, auscultation of the heart has been neglected."

As more and more diagnostic laboratory tests were devised, warnings were issued by leading medical educators. Thus Cushing[3] remarked, "We have instruments of precision in increasing numbers with which we and our hospital assistants at untold expense make tests and take observations, the vast majority of which are but supplementary to and as *nothing* compared with the careful study of the patient by a keen observer using his eyes and ears and fingers and a few simple aids." And Blumer[4] emphasized, ". . . no matter how many technical methods are invented, there will never be a time when a careful history and a competent physical examination will cease to be the foundation for the clinical investigation of disease."

A few recent examples of neglected fundamental methods of examination cast doubt on any claims that progress has been made in the solution of this problem. Redlich[5] and his associates studied the delays and errors in 100 proved cases of brain tumor. Only 4% correct diagnoses and 2% doubtful diagnoses were made by the physicians who first examined the patients. White and Elkin[6] analyzed the low salvage rate in patients with primary malignant bone tumors (of 93 patients, 8 recoveries) and concluded that some costly delays were due to the initial erroneous diagnoses of "arthritis," "rheumatism" and "sprain." Graham[7] estimated that nearly 50% of patients with bronchiogenic carcinoma were diagnosed as having virus pneumonia before admission to his clinic.

The aftermath of past discoveries does not compare in magnitude with the revolutionary changes that have followed the use of the new antimicrobial agents. It is now possible in the treatment of a disease such as pneumonia to make only a single casual examination of the patient, to give scant attention to physical signs, to disregard almost entirely the details of diet, the administration of fluids, and general nursing supervision, and to obtain results that are more remarkable than were ever imagined by the greatest clinicians of the past. And in the surgical specialities, chemotherapy may bring about a complete recovery, for example, in a case of appendicitis despite a delay in diagnosis, mediocre operative technic, and faulty pre- and postoperative treatment. It is difficult to predict the end result of such experiences. Excellent articles on the abuse of antibiotics continue to appear but it is apparent that their use is beyond control. Not only do both patient and physician demand a drug for each disease but also for each symptom. Wier Mitchell's[8] statement that all along the history of medicine, the really great physicians were peculiarly free from the bondage of drugs remains true but defies interpretation to the present generation of medical students.

Knowledge of sensitivity reactions, toxic manifestations, the modification and masking of symptoms, the problems associated with resistant strains of organisms and the evidence of possible permanent physiologic alterations is only imperfectly acquired in respect to one

drug when another is introduced. The more rapid the introduction of new drugs, the greater the number of clinical mistakes. Their life saving qualities, however, makes early release of information imperative. The introduction of a new drug must of necessity be followed by considerable clinical experimentation. This is not harmful to the judgment of mature physicians but is often incompatible with instruction to students and internes in therapeutic conservatism. Treatment without adequate indications and without a careful evaluation of each patient's status is now so prevalent that its future correction is doubtful.

This entire subject has posed new problems in teaching. Many recent graduates have never witnessed the natural course of such infections as pneumonia, mastoiditis or peritonis. They are familiar with the course as modified by the antimicrobial agents. Only the older physicians have observed both the modified and unmodified course of disease. It is difficult to know if exact knowledge of the unmodified course of many infections is essential for the proper guidance of therapy and to what extent it should be retained in new textbooks. In the revision of teaching material, the sections on infections that respond to therapy will eventually be shortened as these disorders and their complications become less important. It is doubtful if such infections will completely be eradicated. Their infrequent occurrence will increase the difficulties in diagnosis and the complexity of teaching schedules. It has been estimated that about 40% of all complaints that require the attention of a physician can now be controlled. Neverthless there is no lack of critically ill patients and serious diagnostic problems. Not only is there no evidence that basic fundamentals can be discarded but the potential dangers of the new drugs make careful bedside observation all the more essential.

Any discussion of the quality of medical care must include the effect of the second world war. The medical students who acquired their education during the war years at understaffed schools and hospitals experienced a training that was not completely satisfactory. Physicians were overwhelmed with a prodigious volume of work. In many instances, only the most important complaints received attention. And in the military service, doctors were stranded medically, so to speak, for three or four long years aboard ship or at some remote station. This upheaval in the medical world was apparent in the years that followed the war. Most important was the effect on the public. Former values disappeared and an inferior type of medical care was accepted by individuals who previously had demanded only the best.

It is generally believed that the level of practice in any community is closely related to the standards maintained in the local hospitals. The quality of medical care within a hospital is dependent upon many factors: the clinical interests of the head of the department, the ability and character of the internes, the attitude and efficiency of the nursing staff, the amount of time available for the care of patients, the physical equipment, and such intangibles as tradition, loyalty and enthusiasm. All are important but of special interest are the changes that have occurred in the daily routine of the internes. At the turn of the century, the house staff had little or no time off and very little or no financial remuneration. Living quarters were provided within the hospitals; matrimony was postponed. There is documentary evidence that this austere existence was a surprisingly happy one. The incidence of illness among the house staff was in part responsible for granting one afternoon off each week, supposedly for the men to obtain the beneficent effects of fresh air and sunshine. Towards the end of the decade preceding the second world war, the amount of time off continued to increase. It became the custom in the majority of

hospitals for the house staff to have every other night off and every other week-end off. Coincident with this change, the yearly stipend increased and what with the war and some unknown factors, marriages became the rule rather than the exception. Living quarters at some distance from the hospital was a necessary consequence. In some insidious way, the night off has recently commenced in the late afternoon. Gradually the personal life of the young physician is becoming of greater importance than his hospital duties. A new factor now influences the attitude of some members of the house staff. The prize of a certificate by a Specialty Board[9] "is such that men planning to devote themselves to medicine rather than to surgery or other specialities requiring technical skills are often motivated in planning their hospital training by getting so many years of credit—putting in time so to speak—rather than by an intrinsic desire for postgraduate study per se." This is not the fault of the Boards. Under normal conditions such men would be dismissed from the hospitals. An unhealthy compromise has resulted from the scarcity of internes due to the exigencies of war.

The daily routine of the interne is an active one and more so today because of the shorter hours of work. There is little time for reading and almost none for contemplation. In the past, the long evening hours permitted time to re-examine patients, to see that orders had properly been carried out, to write intelligent progress notes, to discuss troublesome cases with the resident physician and to re-establish faith and courage to face the future in patients with disabling diseases. With half the house staff away each night and the other half often occupied with new emergencies, the difficulties of furnishing excellent medical care are insurmountable. Miss E. Kathleen Russell[10] in her review of the nursing situation refers to the devastating effect felt by good nurses when they do not have time to nurse their patients properly. The conscientious interne now finds himself in a similar position of frustration. And in the background, the hospital board of directors must make every effort to keep each bed occupied in order to improve the institution's financial status.

Great changes have occurred in medical education during the past 50 years. In 1900 most of the teaching was done by volunteer practitioners without financial remuneration. The advent of the full-time system[11,12] in 1913 provided opportunity for teachers and investigators to devote their entire time to their respective departments. The immediate success of the full-time system was due, in part, to the fact that the men were excellent clinicians. Many departments were strengthened by the participation of part-time colleagues who were actively engaged in practice. As the scope of investigative work widened, the men preparing for academic careers found that it was necessary to transfer their activities from the bedside to the laboratory. In the choice of professors, more attention was paid to research ability. Discord resulted as the balance between clinical medicine and research was disturbed. This is apparent in Herrick's[13] statement: "There should be no quarrel with research per se. There is no higher type of work. It is the activating, catalysing agent in the science of medicine. Without laboratory experimental research, medical science will stagnate and the art of medicine will revert to its old status of empiricism. Yet many research men or, should I say, many men who are working in research laboratories or wards, become poor practitioners." Laboratory and administrative work, lecture tours, local, national and international medical activities have gradually increased to a degree that interferes with the care of patients. Some clinical professors rarely participate in outside consultations and are out of touch with the point of view and needs of the practitioner. Complete daily ward rounds by department heads is almost nonexistent. Ward rounds by

younger members of a department represents time taken from research and since promotion is based principally on scientific achievement, the clinical work frequently suffers. Unfortunately today very few members of a department who are actively engaged in private practice have both the ability and the time for hospital work. In many institutions, ward rounds have become interesting academic exercises in which no senior member of the staff assumes responsibility for all the details connected with the patient's welfare. The rewards that come from an absorbing interest in clinical medicine are unknown to many teachers. The factors that interfere with clinical work similarly affect teaching activities. The situation has been summarized in a recent editorial[14]: ". . . The young man who aspires to become a teacher believes only that in order to succeed he must produce in research; and that only through this channel can he succeed. . . . How can a teacher devote his best energy to teaching when he knows that other considerations shape his destiny more importantly? It is not only that personal achievement may perish if he fails to pursue his avocation with vigor: the reputation of his school may also suffer."

In hospitals associated with teaching institutions, the creation of clinics and wards for special groups of patients has been responsible for a tremendous increase in knowledge. Such innovations have dangers as well as benefits. Prolonged emphasis on diseases with potentialities for research results in neglect of the common ailments. As early as 1928, Peabody[15] warned that these special clinics should not be developed ". . . at too great expense to the general ward lest the general ward come to contain nothing but what are regarded as 'uninteresting cases,' and the idea of specialization be instilled in student and staff too young. After all 'intensive training' does not involve the study of many patients of a group at one time and the rest can be left in the general ward, which should be as exciting in its variety and unexpected manifestations of disease as is the actual practice of medicine." The rotation of internes through special wards or special outpatient clinics at intervals of 6 to 8 weeks remains a complex educational experiment. It does not take into consideration the variable rate at which young physicians approach medical maturity and risks the serious disadvantage of exposing them to the refinements of a specialty before the fundamentals have been mastered.

From time to time the course of events has been discussed by medical educators. In the fascinating atmosphere of highly dramatic scientific discoveries and in the rush of daily life, the comments of these writers have been quickly forgotten. More recent articles contain a sense of urgency in respect to the solution of this problem. An editorial[16] of August 1951 states that ". . . the profession of medicine has had once again brought to its attention a growing suspicion that its science is running away with its art; that its relations with the people whom it serves are not always as close or as agreeable as they should be and that the hour may be later than it seems."

Admiration for the past does not imply hostility towards present day advancements. The accomplishments of the clinical departments during the past two decades are proof that the old days were not the best. The mistake lies in simple acknowledgement of former benefits without the actual incorporation of those benefits in today's progress. The point of view that the passing era of clinical perfection represents a moment of civilization en route for oblivion is a grave error. The solution of the present difficulties is best accomplished by an addition to the existing regime rather than by any change in the established structure. It demands the appointment in clinical departments of a physician who will devote his entire time to the care of patients. His work and his teaching would be carried out at the bedside. He would have the privilege of outside consultations. Above

all he must be free of any obligation to produce in research. His qualifications would consist of a "broad clinical experience acquired by many years of hard work." His appointment should have priority over all other departmental obligations, and where financial difficulties exist, the budget must elsewhere be curtailed. The urgency is due to the increasing scarcity of individuals eligible for such a position. The need is immediate.

References

1. Thayer, W. S., Individualism in medicine, California & West. Med. **31**:377, 1929.
2. Levine, S. A., Diagnostic value of cardiac auscultation, J.A.M.A. **141**:589, 1949.
3. Cushing, H., Medicine at crossroads, J.A.M.A. **100**:1567, 1933.
4. Blumer, G., President's Address, Tr. A. Am. Phys. **58**:1, 1944.
5. Redlich, F. C., Dunsmore, R. H., and Brody, E. B., Delays and errors in diagnosis of brain tumor, New England J. Med. **239**:945, 1948.
6. White, G., and Elkin, M., Primary malignant bone tumors, New England J. Med. **245**:351, 1951.
7. Graham, E. A., Some questions about bronchiogenic carcinoma, New England J. Med. **245**:389, 1951.
8. Mitchell, W., cited in Sir William Osler, by H. Cushing, London, Oxford University Press, 1925, vol. 1, p. 359.
9. Editorial, Education of family physician, New England J. Med. **241**:248, 1949.
10. Russell, E. Kathleen, Medicine as social instrument: Nursing, New England. J. Med. **244**:439, 1951.
11. Janeway, T. C., Outside professional engagements by members of professional faculties, J.A.M.A. **90**:1315, 1928.
12. Dock, G., Full-time clinical departments, South. M. J. **15**:1020, 1922.
13. Herrick, J. B., Practitioner of future, J.A.M.A. **103**:881, 1934.
14. Editorial, Goodbye, Mr. Chips? New England J. Med. **245**:116, 1951.
15. Peabody, F. W., Soul of clinic, J.A.M.A. **90**:1193, 1928.
16. Editorial, To comfort always, New England J. Med. **245**:192, 1951.

3875 Wilshire Boulevard

TRENDS

By John P. Hubbard, M.D., *Contributing Editor*

Statements appearing in this column do not necessarily reflect the opinion of the editor nor are they to be interpreted as the official opinion of the Academy.

HEALTH SURVEY PROPOSED*

LAST week President Truman announced the creation of a Commission on the Health Needs of the Nation that he said would "make a searching inquiry into the facts and give us the benefit of objective and constructive thinking on these problems which are of vital concern to every American."

This newspaper in editorial comment last Sunday welcomed the President's move, saying that the new commission "should be a forward step toward breaking the deadlock that has existed on constructive action for a positive health program." The editorial added:

"The ability, stature and reputation of the new commission, which is to be headed by Dr. Paul B. Magnuson, insure the professional knowledge and maturity of judgment that will be needed to make workable recommendations for solving these problems. It is a commission in which both the public and the health professions can have confidence."

The day the commission membership was announced, however, one appointee, Dr. Gunnar Gundersen, La Crosse, Wis., a member of the board of trustees of the American Medical Association asked that his name be removed from its membership. He said, "I believe I am correct in assuming that the commission is designed, both in its majority membership and its objectives, as an instrument of practical politics to relieve President Truman of an embarrassing position as an unsuccessful advocate of compulsory health insurance."

The following day, Dr. John W. Cline, President of the American Medical Association, termed the commission "another flagrant proposal to play politics with the medical welfare of the American people."

Commission Head Praised

A review of the membership of the commission and of its frame of reference make Dr. Gundersen's and Dr. Cline's accusations difficult to understand. Its chairman, Dr. Magnuson, is noted among medical circles as a critic of bureaucracy, a foe of red tape, and an outspoken opponent of compulsory health insurance.

Nor does the membership of the commission give credence to Dr. Gundersen's and Dr. Cline's assertions. It includes:

Chester I. Barnard, president of the Rockefeller Foundation, New York.

Dean A. Clark, M.D., general director of the Massachusetts General Hospital, Boston.

Evarts A. Graham, M.D., surgeon, St. Louis.

Joseph C. Hinsey, Ph.D., dean of the Cornell University Medical College, New York.

* From "Fight on Truman Health Unit as Political Held Unjustified," by Howard A. Rusk, M.D., *The New York Times*, Jan. 6, 1952. Reprinted in full with the permission of the publisher.

A. J. Hayes, president of the International Association of Machinists, Washington.
Charles S. Johnson, president of Fisk University, Nashville.
Russel V. Lee, M.D., Associate Clinical Professor of Medicine, Stanford University School of Medicine, Palo Alto.
Elizabeth S. Magee, general secretary of the National Consumers League, Cleveland.
Clarence Poe, president and editor of *The Progressive Farmer,* Raleigh, N.C.
Lowell J. Reed, Ph.D., vice president of the Johns Hopkins University and Hospital, Baltimore.
Walter P. Reuther, president of the United Automobile Workers, C.I.O., Detroit.
Marion W. Sheahan, R.N., director of the National Committee for the Improvement of Nursing Services, New York.
Ernest G. Sloman, D.D.S., president-elect of the American Association of Dental Schools, San Francisco.

In announcing the new commission, President Truman did not refer to his past proposals for Federal health insurance directly, but said: "On a number of occasions I have stated that I would be happy to consider constructive suggestions which were better than the proposals I have endorsed to bring the continuing achievements of medical progress to all of our people. They have not been forthcoming."

Unanswered Problems Listed

He termed the many vital problems that remain "unanswered" as:

1. Insuring an adequate supply of doctors, nurses and allied personnel.
2. Developing local public health units.
3. Making more hospitals, and hospital beds available where needed.
4. Stepping up the tempo of fundamental medical research.
5. Meeting the needs of the chronically ill and aged.
6. Providing adequate diagnostic, rehabilitative and other medical services to all income groups regardless of financial ability.

As to the commission's being a program of "political propaganda" as the A.M.A. officials have charged, it is significant that, although it will give interim reports, the commission has 12 months to complete its studies. Thus, its terminal date is well after the 1952 elections.

Certainly no one can disagree with Dr. Cline's statement that the "health of the American people has never been better." One of the greatest achievements of this nation during the past half-century has been in the general improvement of the health of our people. From an average lifetime of 49.2 years in 1900, our life expectancy has risen by more than one-third to nearly 68 years.

This hardly seems in conflict with the President's statement that "We still have a long way to go, however, before we can hope to provide for the health needs of our people on both an immediate and long-time basis."

Statistics of Needs Noted

Statistics are cold, but, when one looks at them knowing that he too will some time be one of these numbers it is difficult to disagree with the President. For example:

1. Estimate of the total number of Americans having some chronic disease, orthopedic impairment or serious defect in vision or hearing have ranged as high as 28,000,000.
2. One out of every 18 persons in the United States is now suffering from some form

of mental illness and one out of every 10 persons will need psychiatric care at some time in his life.

3. About 20,000,000 people now alive will die of cancer unless new treatments and cures are found.

4. This year approximately 775,000 persons will die of diseases of the heart and circulation.

5. Two persons out of three in the United States need financial help to meet the costs of serious illness.

These are but a few of the many unsolved problems. Currently blocking the way to their possible solution are many other problems. For example:

1. Sickness absenteeism costs the nation the full time of 2,000,000 workers each year

2. The nation's medical schools are faced with a serious financial crisis. Their deficits in 1948 totaled $10,000,000 and are running higher today.

3. Nearly 50,000 nurses over and above those now in sight will be required by 1954 to meet both civilian and defense needs.

4. Nearly 30 per cent of our citizens live in communities in which there are no full-time local public health services.

It is obvious that today we do not have the solution to many of these problems. It seems reasonable to assume, however, that a high caliber commission of this type, representing both the producers and consumers of medical services, should have much to offer to the benefit of both patients and physicians. It would be tragic indeed if full cooperation is not given to them in their efforts.

PUBLIC HEALTH, NURSING AND MEDICAL SOCIAL WORK

MYRON E. WEGMAN, M.D., *Contributing Editor*

HEALTH SERVICES FOR SCHOOL CHILDREN—PRIORITIES AND PROGRAM

IN DECEMBER 1951 a general discussion of the significance of organized health services for school children was presented in this column, using certain specific health problems for illustration.[1] Two recent reports, "Priorities in Health Services for Children of School Age"[2] and "Report on the First Session of the Expert Committee on School Health Services, World Health Organization,"[3] were cited at that time. Both of these have material of considerable interest to practicing pediatricians and child health workers.

The "Priorities" statement, published by a joint committee of the Children's Bureau, Public Health Service and Office of Education, presents the results of the deliberations of a group of consultants who met in Washington in the summer of 1949. The group included physicians, nurses, teachers and health educators. They addressed themelves particularly to the matter of assessing the factors which would determine what services should take precedence as a program gets under way, or when limited funds and facilities are available.

At the very beginning this report points out that the phrase in the title—Health Services for Children of School Age—was chosen to emphasize the fact that such services stem from the community as a whole. Furthermore, "Parents have primary responsibility for the health of their children. Health service programs should be designed to assist parents in discharging this responsibility but not to assume it for them.

"Fullest possible use should be made of the family physician and dentist in the health service program.

"Health service programs carry with them great significance for education for all concerned. Physicians, dentists, nurses, and teachers need to be continuously aware of this function and their obligation to derive from the health services their fullest educational value for the children and community.

"The younger a child is when any abnormality is discovered and treated, the more benefit will he derive in terms of school progress. Other things being equal, therefore, any programs designed for children of school age should aim first at the younger age groups."

Planning: The report lays great stress on the need for careful, joint planning as a prerequisite for success. In even the most limited situations, where there might be no health department or public health nurse, a surprising number of groups and individuals have concern with the health of children. Besides the parents there are physicians, dentists, teachers, welfare workers, voluntary health groups such as the Red Cross and the Tuberculosis Association, service clubs and others.

On the subject of planning, some excerpts from the report of the World Health Organization Expert Committee are also apropos.

"Planning is a team project, involving parents, community, professional groups, social

agencies, and all interested in the welfare of the child. Planning should include everyone who is going to have any connexion with the programme. Those who are in the planning from the beginning cannot help but have a better understanding of aims, standards, and methodology. Organization of a health council to give form to the mutual planning has been shown to be a helpful device. . . . It hardly needs to be emphasized that planning should be based on the local situation and not on a stereotyped pattern.

"An example of effective planning is found in the integration of school health services with other services, such as those for infants and pre-school children, the work of the public-health departments, and the services of general practitioners and hospitals. Effective supervision of growth and development demands continuity. A programme of health services for schoolchildren should be a direct continuation of pre-school services and should be so correlated that the benefit of information about the child accumulated during the pre-school period may be available in the school health programme.

"In some parts of the world, health workers are faced with vast areas having a formidable incidence of endemic and epidemic diseases, an almost total absence of sanitation, and ignorance of personal and community hygiene. There is great opportunity for campaigns of mass treatment and institution of sanitation projects; but such a programme alone is one-sided. It must be emphasized that most lasting improvement in public and individual health will come through changing attitudes and developing understanding—in short, through education. As much as possible should be done by the people, by their cooperative action, and as little as possible by unexplained intervention."

Environmental Hygiene: Both reports emphasize the fundamental importance of a healthy environment particularly from the standpoint of educational implications. A child learns more from what he actually sees and experiences than from what he reads in books. Expensive installations are not necessary. "A carefully protected spring or properly cleansed containers for carrying water may be far safer than pipes and faucets involving cross-connexions. Similarly, a well-built and well-kept latrine may be far safer as well as of greater fundamental educational value than a porcelain and tile toilet which is allowed to become dirty and a nuisance. It is often stated that rural communities with limited resources may be seriously handicapped from the standpoint of environmental sanitation. While this may be true in relation to ease and comfort, or to aesthetics, it is entirely feasible for such a community to achieve satisfactory standards of safety and to encourage good hygienic practices."

Nutrition: The role of the school in this field was considered by the W.H.O. Committee both from the standpoint of direct benefit and education. "Sound nutrition is closely related to educational progress; the poorer the nutrition, the more difficult it is for the child to learn and to cope with school life. Undernutrition is a serious obstacle to promotion of physical and mental health. . . . Any scheme of school feeding must be accompanied by education in the principles of nutrition related to the food used. To carry out this task teachers need adequate preparation. . . . The committee felt that schools, particularly in areas of low economic status where nutrition is likely to be poor, have a very important function in providing needed nutritional elements through meals taken at schools."

A possible danger in regard to nutrition, particularly where food is scarce, is "that the meal at school will be regarded by the parents as adequate or nearly adequate for the whole day. Wherever this occurs, the benefits of the school meal may be offset by virtual starvation at home."

The W.H.O. report deals with other items of health promotion such as the school day, safety control, health supervision of school personnel and communicable disease control. The desirability and benefits of directed physical activities for all children are discussed briefly. Medical review is advocated in order to advise the proper grade of activity and at the same time to discourage excuse from all activity.

Mental Health: Three obstacles in this important field are cited as requiring attention: (1) lack of interest on the part of school health workers, (2) insufficient training and (3) too little teamwork within the school and community. "Another factor affecting the health of children and one too often given inadequate attention is the 'emotional climate' of a classroom. The personal warmth of the teacher, the permissiveness of class procedures and wise administration of tests, grades, and promotions contribute to the way a child feels about himself and school." Preparation of teachers with due regard for mental health involves encouragement of sympathetic and warm attitudes as much as presentation of facts.

Health Education: While this is implicit in all health work for school children, it also needs to be included as an explicit part of the instructional program. Use of visual aids, of local resources, of information from physician and nurse concerning particular health problems in the school or area, and of specific school projects with direct student participation, are all described as important aids to effective teaching. Training of physicians and nurses, as well as teachers, must be directed toward effective health instruction. Many communities make extensive use of specialists in health education called "health educators" for "developing health curricula for various grade levels, and in-service courses and institutes of health for teachers; coordinating the health services and health instruction in the school; and in helping school health councils to function effectively.

"One controversial problem in health education is presented by what is popularly called sex education. It appeared to the committee that this subject comprises two separate problems. The first is the task of aiding the child to acquire knowledge of sexual physiology. This objective, the committee felt, should be an integral part of the general teaching of human physiology which health instruction should include.

"The second problem is that of enabling the child to develop a capacity for responsible behaviour in sexual relations. This appeared to the committee to be one part of the general problem of devising methods of education which assist the child to learn how to establish relations with other human beings which are in all respects harmonious and responsible."

Health Appraisal: Both reports present approaches along the lines presented in the previous column. The best use of available professional time is obviously of primary concern. The "Priorities" statement suggests the following order as reasonable and desirable for the various steps of a health appraisal program.

1. Continuing preparation of staff by means of joint planning, conferences, workshops, visits and institutes
2. Health history
3. Continuous alert teacher observation
4. Certain specific screening tests to be made, preferably by teacher or technician
5. Record keeping
6. Medical examination
7. Special consideration of athletes. Athletes are ordinarily among the healthiest

segment of the school population and therefore should not receive a disproportionate share of available health service for the school-age child.

The problem of physical examinations and periodic review received detailed attention in both reports with essentially similar conclusions.

"The physician's responsibility in relation to health supervision needs careful evaluation. The committee believed that health appraisal is the cornerstone of health service for the child of school-age. The continuous observation by teachers, discussed in the previous section, combined with the objective measures described as 'screening' tests, form the basis for effective health appraisal. The activities of physician and nurse in instructing the teacher in proper performance of these functions have a high priority and can be as rewarding as any phase of medical and nursing activity in the school.

"When a nurse serves the school she can collaborate with the teacher through prearranged, organized teacher-nurse conferences, to provide annual or semi-annual review of the health status of every child in the class. From this preliminary health appraisal those children most likely to need care can be selected for the physician's attention. Caring for these cases should receive priority in using the time the physician has allocated to school health examinations. Experience has demonstrated that medical examinations are particularly fruitful when the student has been specifically referred to the physician because parent, teacher, or nurse suspected that something was wrong.

"Physical examination, carried out at periodic intervals with care, on the basis of adequate history, with parents present and with sufficient time for the physician to carry out his function as a counsellor in health and a teacher for parent and child, is a highly valuable procedure and one of the fundamental parts of a complete school health service. The committee questioned seriously, however, the value of the all-too-common cursory medical inspection carried out as routine. Medical examinations should be sufficiently painstaking and comprehensive to command medical respect; sufficiently informative to guide school personnel in the proper counselling of the students; and sufficiently personalized to form a desirable educational experience. In the younger age-group, the school should make an unusual effort to announce and schedule medical examinations at such times and places that a parent can attend the examination and have the benefit of the physician's immediate recommendations concerning the health of the child.

"When planning the use of the physician's time available for schoolchildren, the various priorities should be provided for properly. The number of periodic examinations to be carried out must be decided after consideration of the time necessary for performance of the functions already cited—advice and consultation to parents, children, and school personnel, and diagnosis and treatment of conditions referred from screening procedures —which take precedence. As physician time becomes available for periodic examinations, newly admitted children should receive attention first, then children leaving school through graduation or for other reasons, then those about the beginning of puberty, i.e., about 13 or 14 years old, and then those about 9 or 10 years old."

Health Restoration: Here is the crux of much of the school health program. Discovery of difficulties represents little gain unless action toward correction results. It was emphasized that a school health service "must consider as one of its functions the securing of facilities for treatment which are available for all school children . . . [and are] fully integrated with the general health services of the area."

Most programs of health services have limited resources, personal and financial, and

selection of conditions to receive priority thus becomes a fundamental consideration. No easy answer is possible and any system of evaluation is open to criticism. The "Priorities" report suggests the use of a series of criteria by which the relative importance of a disease condition might be judged. The criteria need to be evaluated in relation to each other as well as in their variable applicability to specific diseases. The statement suggests the possibility of a direct numerical approach describing the suggested method in detail and giving examples indicating advantages and disadvantages.

The need for making criteria discriminating is obvious. Effects of a disease on nutrition is unquestionably important but since such an effect will apply to almost all disease the criteria will not serve to distinguish.

"Furthermore, while the criteria will indicate conditions to receive attention first, they do not imply that a given community should not attempt to care for conditions not ordinarily selected by these criteria. They do imply that care of such conditions should not be undertaken until adequate provisions exist for the care of those with a higher priority.

"A corollary problem in relation to care and treatment is the need for developing policies to govern desirable extent of care to be given for conditions selected by the criteria proposed. The necessity is particularly great in regard to such problems as dental care, one of great magnitude.

"With these premises in mind, it is suggested that the priority a condition should command in regard to care and follow through of children of school age would depend upon the degree to which the condition:

(a) Interferes with satisfactory progress in school;
(b) Affects unfavorably the emotional status of the child;
(c) Is amenable to preventive measures;
(d) Is progressive to a serious handicap or disease or is likely to affect the eventual health of the child;
(e) Is common to many children throughout the country or is peculiar to the specific community;
(f) Endangers the health of others in the family or community;
(g) Is correctible by medical treatment;
(h) Requires limited expenditure of funds per case;
(i) Has been neglected in the past;
(j) May be adequately treated by facilities and personnel which are or can be made available.

"It was the sense of the committee that when these criteria are used in connection with a program for the child of school age in which a limited service is financed by other than individual family resources, treatment of acute diseases should in general be considered as outside the scope of the program."

True usefulness of these criteria must await practical trial. They do, however, represent an interesting tool which may be very serviceable.

The importance of dental health was recognized by both groups but neither felt competent to give the subject the extensive treatment it deserved.

Health records will be most practical and useful if certain principles in their construction and use are followed. They need to be cumulative, to contain information prior to school entrance, to show progress in health objectives and growth and to be couched in language which can be understood by those who will use the records. The

staff to use the records should participate in their construction and be trained in their use. "Certain information contained in school health records may be tabulated because of their usefulness in guiding administrative policies. Statistical summaries of diagnoses, however, can be undertaken with confidence only when diagnostic criteria are standard and uniformly understood, when provision is made for both positive and negative statements regarding the diagnosis or diagnoses under consideration, and when periodic evaluation of the accuracy of the statements on the records can be undertaken. Since school health records involve such a large number of persons, the committee felt that further study of ways and means of using these records for collection and analysis of important data was well merited."

Administrative Framework: Organization of health services within the schools frequently presents jurisdictional difficulties. It is often stated that health departments have responsibility for community health services for *all* the people, while educational authorities have responsibility for *all* activities going on within the school. This apparent contradiction can be resolved only through mutual understanding and cooperation. The Expert Committee enunciated a series of principles:

"1. Great variation in forms of administration is possible, and no standard framework can be devised to meet the circumstances of all countries.

"2. Efficiency of the school health work will ultimately depend less upon the particular framework of administration than upon the manner in which the school health teams discharge their responsibility and bring about a material understanding in cooperation with all other authorities who share services related to school work.

"3. In view of the importance of this cooperative relationship, the committee stressed the great advantage which will be derived from integrating the administration of the school health service with the administration of the general community health programme. This can be achieved when the medical officer in charge of community health is also the school medical officer and, no doubt, in other ways.

"4. The school medical officer (and other staff in the school health team) must have a definite assignment which will place him in a position of responsibility towards the maintenance of health in the school. He must not in any circumstances be regarded as an occasional visitor with no continuing responsibility.

"5. Sound relationships between the school health team and the family and the community (of which the school is a part) will be furthered when the nurse serving the school serves also the general health needs of the community. Where this is impractical, administrative provisions between departments should permit the nurse working in the school to share in the work and professional meetings of the community health workers.

"6. A school health service should serve all children of school-age in a defined community and therefore should include children attending private schools.

"7. Health services for children of school-age cannot be isolated from community health care in general; this is particularly true of maternal and child health activities. A good school health service, therefore, will be correlated with the child services for the pre-school years through some such means as having the school health staff work also in the maternal and child health service. The same principle is true for the period after leaving school, and the school health service should be correlated with such general health services as industrial hygiene and appropriate clinics.

"8. Reference was made earlier to the desirability of school health councils or committees. Their organization can bring together all in an area who are interested in

school health—parents, industrialists, and social workers, in addition to the more directly involved professional personnel. In smaller communities, where the school is a centre of community activity, the village health committee may well function as a school health committee.

"9. The committee stressed the importance of the total and continuing child health concept. Prenatal work, infant-welfare centres, preschool health services, school health work, and health supervision of adolescents should be guided by the same medical administration, in order to obtain uninterrupted continuity in the supervision of the individual during the whole period of growth and development. Where, however, it is administratively impossible or inadvisable to follow this procedure, responsibility must be assumed by the different agencies involved so to co-ordinate their work that the health guidance of any child is not fractionized."

Both of the reports which have been discussed are concerned with health services in small communities with limited resources as well as larger and wealthier communities. The material can be most helpful to all who are prepared to think about health services for school children critically.

References

1. Wegman, M. E., Health services for school children, PEDIATRICS 8:851, 1951.
2. Priorities in Health Services for Children of School Age, Washington, D.C., Federal Security Agency, n.d., 24 pp.
3. Expert committee on school health services, report on the first session, World Health Organization, Technical Report Series no. 30, April 1951.

NEWS AND ANNOUNCEMENTS

The Louis Lefkoe Memorial Foundation offers a prize of $500 for the most worth while original contribution to the medical knowledge of cerebral palsy.

The paper is to be in the customary format for publication of medical literature. It may cover any aspect of the subject, such as pathogenesis, biochemical knowledge, pathology, diagnosis or treatment. The paper is to submitted to the trustees of the Foundation on or before Sept. 1, 1952. The prize is open to anyone who can contribute to the medical knowledge of the subject.

Address: The Louis Lefkoe Memorial Foundation, 601 Medical Arts Building, Sixteenth and Walnut St., Philadelphia.

* * *

MEMORIAL CENTER FOR CANCER AND ALLIED DISEASES

The Pediatric Department announces a comprehensive 3 day course May 21, 22 and 23, 1952, for pediatricians, general practitioners and health officers. Current developments and established methods in diagnosis, differential diagnosis and management of benign and malignant tumors, Hodgkin's disease, leukemia and reticuloendothelioses in childhood are included.

Content of course: Demonstrations, examinations of children in Pediatric, Surgical, Chemotherapy, Radiotherapy Clinics; Ward rounds and Seminars under the direction of the Staffs of Memorial Hospital and Sloan-Kettering Institute for Cancer Research. Fee $35.00.

For information address: Director, Pediatric Service, Memorial Center, 444 E. 68th St., New York City.

* * *

Announcement is made of a 2 weeks' postgraduate course in General Pediatrics, Burnham Memorial Hospital for Children, Massachusetts General Hospital, Boston, under the auspices of the Harvard Medical School, June 9 through June 21, 1952. Clinics providing a broad review of pediatrics emphasizing the new advances will be given daily from 9:00 a.m. to 4:30 p.m. by selected authorities from the Pediatric and Specialty Services of the Massachusetts General Hospital, the Ophthalmological and Otolaryngological Services of the Massachusetts Eye and Ear Infirmary and the Children's Medical Center, Boston. For further information write: Assistant Dean, Courses for Graduates, Harvard Medical School, 25 Shattuck St., Boston.

* * *

A summer camp for diabetic children will be opened for the fourth season under the auspices of The Chicago Diabetes Association, Inc., from July 1, 1952, to July 22, 1952 at Holiday Home, Lake Geneva, Wis.

In addition to the regular personnel of the camp, there will be a staff of dieticians and resident physicians, trained in the care of diabetic children, furnished by the Chicago Diabetes Association. Boys and girls, ages 8 to 14 years inclusive, will be accepted at a fee of $120.00 (which covers the 3 week camping period and transportation from Chicago). Fee reductions may be arranged when considered necessary.

Physicians are requested to notify parents of diabetic children and to supply the names of children who would like to attend camp. Applications may be obtained from, and inquiries should be addressed to: Service Unit, Chicago Diabetes Association, 110 S. Dearborn St., Chicago.

* * *

The University of Minnesota will present a course in pediatrics on April 21 to 23, 1952. The course will be presented at the Center for Continuation Study and is intended primarily for physicians specializing in pediatrics. Emphasis will be placed on infectious diseases as they occur in pediatric practice.

Dr. John M. Adams, Professor, Department of Pediatrics, University of California, Los Angeles, formerly a member of the Department of Pediatrics at the University of Minnesota, will deliver the annual Clarence M. Jackson lecture sponsored by the Phi Beta Pi Medical Fraternity on the subject of "Respiratory Diseases—Changing Concepts."

For further information write: Robert B. Howard, M.D., Director, Department of Continuation Medical Education, 3330 Powell Hall, University of Minnesota, Minneapolis.

* * *

Dr. Francis R. Janney of Milwaukee died on Oct. 21, 1951. He was a fellow of the American Academy of Pediatrics.

* * *

Dr. Robert A. Black of Chicago died on Jan. 13, 1952. He was a fellow of the American Academy of Pediatrics.

BOOK REVIEWS

PEDIATRIC ALLERGY, Robert Chobot, M.D., New York, McGraw-Hill Book Company, 1951, $4.50, 284 pp.

The author states in his preface that this book was written for the student taking a course in pediatric allergy, and for the pediatrician and general practitioner, and that he has tried to strip away all excessive wordage and to use straightforward, simple language. He has succeeded admirably in his purpose. The book is short; it is less than a complete discussion of pediatric allergy, more than an outline, and it is an excellent example of how a clear-headed and common sense writer can boil down a complicated subject, without leaving out much that is essential.

Dr. Chobot's discussion of skin testing is excellent, and should be studied carefully by all novices in allergy. The reviewer, however, does not agree with him in his use of the intracutaneous test before scratch tests have been done, and the fact that he devotes 2 pages to the treatment of constitutional reactions which may follow intracutaneous testing suggests pretty strongly that constitutional reactions not uncommonly follow intracutaneous testing. In the reviewer's opinion no intracutaneous test should be done on anyone, child or adult, unless a scratch test has been done first and is negative. Altogether too many deaths have been reported from primary intracutaneous testing.

Dr. Chobot devotes a considerable amount of space to a discussion of respiratory infection in its relation to asthma—he believes that it is of the utmost importance. The reviewer agrees with this. One is left with the impression, however, that this problem is solved in a high proportion of cases by removal of the tonsils and adenoids. This is quite contrary to the reviewer's experience and to that of most other allergists and pediatricians.

There is an appendix containing 27 case reports: there were 100% cures or near cures, which gives a too rosy picture of the practice of allergy. It is a pity that someone doesn't write a paper sometime analyzing his failures; there are plenty of them. The author recommends immunization by injection for poison ivy and also phylactic treatment. Most dermatologists have come to the conclusion that immunization is of questionable value, and that phylactic treatment should not be used, that it is likely to do more harm than good.

Notwithstanding these few criticisms, the reviewer considers this to be a valuable book for any beginner in allergy. It is full of clearly expressed information and sound common sense. It is recommended to pediatricians interested in allergy as the first book to buy; then as they become more familiar with the subject they can turn to one of the larger books, such as those written by Tuft, Feinberg, Vaughan or Urbach.

SPECIFIC DYSLEXIA: CLINICAL AND GENETIC STUDY, Bertil Hallgren, Acta Psychiatrica et Neurologica, Supplementum 65, Copenhagen, Egnar Munksgaard, 1950, 287 pp.

The objectives of this study (done at the Psychiatric Clinic of the Karolinska Institute, Stockholm, between 1947 and 1950) were to determine the possible existence of an hereditary form of specific dyslexia and through a clinical analysis to discover something about the mode of inheritance. The role of certain extraneous factors was also to be considered. The case material consisted of 79 children from the Stockholm Child Guidance Clinic diagnosed as having specific dyslexia plus 43 children from the special reading classes of a secondary school. This group was compared with a group of 212 children from the 3 lowest classes of another school.

The first part of the monograph is concerned with a careful analysis of factors which might contribute to difficulty with reading. It is important to distinguish between primary or "specific" dyslexia and reading or writing difficulties of a secondary nature. Some children have trouble with their reading because of low intellectual capacity, physical illness, frequent changes of schools, poor teaching, undesirable home environment, emotional disturbances or neurologic disorders. These children do not as a rule show a disparity between reading achievement and success in other school subjects. Hallgren does not believe that there is adequate evidence for any significant relationship between poor reading and visual defect nor does there seem to be any true causal relationship with faulty eye movements. There was a high incidence of nervous disorder in the child guidance clinic cases but it was not strikingly high in the group from the remedial classes.

After a careful consideration of all the aspects of the association of speech defects and left-handedness with reading difficulties, Hallgren concludes that, at least in boys, there is a direct association between speech defects and specific dyslexia. Even with a relatively crude method of identifying laterality, left-handedness was more frequent in the children with specific dyslexia than in the control group.

Hallgren finds that there is a 10% incidence of specific dyslexia in the general population. In 88% of the cases with specific dyslexia there were one or more members of the family with the same difficulty. In the analysis it is pointed out that the mode of inheritance is most probably monohybrid autosomal dominant.

There are numerous clear tabulations of the author's collected data. More than 225 references are listed and many of these are quoted in the discussion. The work has been carefully done. The English translation is good.

This study is of both general and clinical interest. It is recommended to anyone who is interested in language disorders.